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EFFECT OF HYPOTHERMIA UPON VITAL STAINING OF THE BRAIN[1]

A Study of the Blood-Brain Barrier

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The importance of hypothermia to neurological and cardiac surgery has led to its widespread investigation. The present experimental trend is toward producing profound hypothermia with the view of prolonging the protection against neuronal hypoxia during surgically effected ischemia of the brain. The effect of hypothermia upon non-neuronal elements of the nervous system has not been reported as yet. However, Broman (3) noted a disturbance of the blood-brain barrier (hereafter called the barrier) during hyperthermia at 45° C. and Laskowski (14) showed that freezing of the cortex results in local dissolution.

It was our objective to gather data on the barrier at brain temperatures between 16° and 20° C. and 5° and 10° C. Further we sought to determine if hypothermia would protect against the passage of agents known to cross the barrier in studies conducted at usual temperature. Methylene blue was used for the latter purpose. Trypan blue was used to examine for increased barrier permeability in hypothermia. Doubts have been raised concerning the use of trypan blue for this purpose. However, maintaining standard conditions and dye concentration and varying only brain temperature, trypan blue proved entirely adequate for our needs. Furthermore, the exact locus and mechanism of the barrier did not appear relevant to our work. There are excellent studies upon that subject and the reader is referred to King (12), Friedmann (8), Tschirgi (21), Rodriquez (18) and Bakay (1).

MATERIAL AND METHODS

In all, 51 cats, five dogs and six puppies were used. Surface cooling of the entire body, or of the head alone, was employed in all but the five adult dogs. The latter were subjected to isolated brain cooling through extra-corporeal perfusion. Rectal temperatures were measured with usual laboratory thermometers, and intracerebral temperatures with a thermistor incorporated into a #20 hypodermic needle. All animals were anesthetized with Nembutal (approximately 30 mg./kg.). Animals used for experiments with profound hypothermia were heparinized, both to lower the critical temperature for cardiac arrest (6) and to facilitate washing of cerebral vessels during supravital studies of the barrier. To solve the respiratory paralysis in profound hypothermia we used a mechanical respirator; thereby barrier changes were avoided which might otherwise have been attributed to anoxia or hypercapnia (7).

Normally certain small areas of the brain have no barrier and hence take up the trypan blue. Thus, each animal provides several control areas to test the efficiency of the injection. These areas include the hypophysis, epiphysis, choroid plexus, area post-

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rema, etc (22). Animals of our series in which these areas did not stain were discarded as inadequate experiments. Controls at normal temperatures were obtained as a check on the technique for each of the groups described below. There is controversy in the literature over whether brains studied supravitally with trypan blue should be perfused with saline prior to removal from the skull. We therefore ran some animals with and some without terminal saline perfusion (4). Further controls consisted of animals in whom the barrier was disrupted mechanically with hot needles (17) or chemically by carotid injection of concentrated angiographic dye (5). To ascertain that the physical effects of the cold alone would not interfere with staining, we injected trypan blue into the cisterna magna (10) of cats with brain temperatures of 20° and 8° C. In each case the brain stained intensely blue.

The brains were processed for histological control. Brains stained with methylene blue were cut into thin slices and passed through cold 6% ammonium molybdate, fixed in 10% formalin, cut at 150 μ, air-dried after mounting in egg albumin, and dehydrated rapidly in alcohol (9). Brains from the trypan blue animals were preserved in either formalin or Heidenhain's Susa fluid, sections were cut at 200 μ, cleared in glycerin and examined either directly or after counterstain with eosin or kernechtrot. In general it was found that the microscopic study added very little to these investigations, and the gross coloration of the brain afforded a better index of the degree, if any, of disturbance in the barrier.

RESULTS

The technique was varied for each of the five groups of animals described below. The result as well as a detailed description of the investigative method for each group follows:

Group I was composed of 18 adult cats studied with methylene blue. A 2.5% solution of this dye was given by slow drip into the aorta via subclavian catheter. In different animals brain temperatures varied between 12°. and 37.5° C. (normothermic). The toxic effects of this dye on the CNS were in no way lessened by the hypothermia. Pupillary dilatation, respiratory arrest, and falling blood pressure ensued rapidly in both normothermic and hypothermic animals if the solution were given with any degree of rapidity. Hypothermia did not enhance or otherwise alter the vital staining process.

Group II was composed of 18 cats in which the brain temperature was lowered to the range of 16.8° to 19.5° C. Eleven of the animals received 4 ml. of 1% trypan blue intraperitoneally on three of four days prior to inducing hypothermia, and all 18 cats received 4 ml. of 1% trypan blue intravenously during the period of hypothermia. Nine cats died or were killed six to 12 hours after the hypothermia had ended. Two cats each were killed 24 hours, 48 hours, and 72 hours after hypothermia. Each of the latter chronic animals received 4 ml. trypan blue intraperitoneally during each 24 hours of survival, and one of each pair was perfused through the aorta with 200 ml. saline followed by 200 ml. formalin at the time of sacrifice.

None of these brains showed any blue discoloration save in the expected areas (hypophysis, choroid plexus, etc.). Control cats at brain temperatures of 20° C. in which the barrier had been broken by concentrated angiographic dyes, did show the staining. It would thus appear that at brain temperatures of 16.5° to 19.5° C., there was neither immediate nor delayed (to 72 hours) breakdown of the barrier.

Group III consisted of a new-born litter of six pups. Three were used at 18 hours and three at 36 hours. One of each trio was used as a normothermic control. Each pup received 1 ml. of 1% trypan blue intraperitoneally at the beginning of hypothermia and ½ ml. intravenously at the lowest point of hypothermia. Hot needles were inserted into the right cerebral hemisphere of one of each pair subjected to hypothermia. The animals

were killed or died after approximately two hours of hypothermia, and each was perfused through the aorta with normal saline followed by formalin. In no instance was there evidence of uptake of the trypan blue. It would thus appear that the barrier of the pup is fairly mature at birth and able to tolerate brain temperatures in the 13°–16° C. range without break-down.

Group IV consisted of 12 cats perfused supravitally according to the technique of Broman (2, 3). The perfusions were carried out at brain temperatures of 2.5°–8° C. Broman's experience showed the barrier remained intact for 6–12 hours after death. We felt, therefore, that even should these animals develop cardiac arrest, a supravital analysis of the barrier by means of carotid perfusion would prove reliable. These animals were heparinized in order to forestall sludging in capillaries, anesthetized with Nembutal and packed in ice. When brain temperatures of 8° C. or less were reached, the chest was opened and the carotids perfused via an aortic cannula. The typical experiment consisted of first washing with 200 ml. saline, followed by 40 ml. of freshly filtered 0.15% trypan blue. Finally the vessels were perfused with 10% formalin following a final wash with 200 ml. saline. The perfusion pressure was kept below 100 cm. of water (2) and care was taken to avoid air embolism, which of itself is known to disrupt the barrier (15). All the brains in this group took up the trypan blue, although usually to a very mild degree. However hot needle tracks, created in one hemisphere just prior to perfusion, had a darker blue appearance than the remainder of the brain which, as stated, colored only to a moderate degree. We would conclude from this series of supravital experiments that a slight disruption of the barrier occurs at 8° C. and below.

Realizing that a supravital study of the barrier is fraught with many possibilities of artifact, we repeated this study intravitally. Three cats were anesthetized, heparinized, tracheotomized and placed on a respirator. The head only of each animal was submerged in ice brine, after first trephining the skull to record brain temperature. One animal had hot needles inserted into one hemisphere. When brain temperatures of 9° C. or below were recorded the chest was opened. At this point the rectal temperatures ranged between 24° and 27° C. The heart was seen to be beating slowly but effectively in each case, and 4 ml. of 1% trypan blue was given intravenously via a femoral catheter. Again, as in the supravital series, the brain of each animal was observed to show a mild but definite blue discoloration. We feel that anoxia, hypercapnia and air embolism (low pressure ventilation) were entirely eliminated in these animals and that the circulation was maintained effectively for at least 10 minutes following injection of the trypan blue. Therefore, we attribute barrier disruption in this group of animals to the profound cerebral hypothermia.

Group V consisted of five dogs subjected to selective cerebral hypothermia by means of blood stream cooling, using an extracorporeal pump and heat exchanger for the carotid circulation. In one animal when the brain temperature had reached 13° C., the perfusate was changed from cooled blood to cooled 0.15% trypan blue, 100 ml. of this solution being given at a perfusion pressure of 240 mm. Hg. and at a flow rate of 80 ml./min. A perfusion of 200 ml. cold saline followed the trypan blue. The brain was removed immediately and found to be uncolored by the dye, *i.e.*, no disruption of the barrier had occurred. An additional four dogs which had undergone cerebral hypothermia by the same method were given 30–50 ml. of 1% trypan blue intravenously 30 minutes before sacrifice. The lowest brain temperature in this group was 8° C., the highest 27.8° C., and the dogs ranged from 18 to 76 days post-hypothermia at the time of sacrifice. None of these brains were blue. Therefore, in this small but sufficient series it appears that there was neither immediate nor delayed disturbance of the barrier during

isolated brain cooling. It may well be that the dog with a brain temperature of 8° C. would have shown a break-down of the barrier during the period of hypothermia, but when tested 18 days later the barrier had regained its normal character.

DISCUSSION

Hypothermia has a profound effect on the CNS. Cerebral blood flow falls and oxygen consumption is decreased (20). Brain volume is diminished and cerebrospinal fluid pressure is lowered (19). Cortical neuronal activity declines and at 20° C. the EEG becomes flat (23). From our studies it would appear that the barrier is unaffected in the range of hypothermia commonly used clinically at this time, but at or below 9° C. partial permeability does appear. This is of particular significance to the neurosurgeon in view of Klatzo's (13) finding that cerebral edema commonly follows a disturbance in the barrier, the edema usually developing in about 12 hours. This might also explain partially the observation by Lougheed and Kahn (16) that grave sensory and motor changes can be present in dogs which survive cooling to 8–12° C.

Grontöft (11) noted an increased susceptibility of the neonatal barrier to asphyxia. In our experiments the barrier of the new-born pup was found to withstand hypothermic brain temperatures of 13–16° C. without passing trypan blue. We interpret this as evidence of a high degree of maturation in the barrier of the new-born dog.

One could hardly expect the efficiency of the barrier to be improved by hypothermia. The fact that methylene blue continues to cross the barrier and exert its toxic neuronal effect during hypothermia substantiates this opinion.

SUMMARY

1. The blood-brain barrier to trypan blue remains efficient at brain temperature of 16° C. and higher in the adult cat; and at 13° C. and higher in the new-born pup.

2. The barrier to trypan blue is partially disrupted at brain temperatures at and below 9° C.

3. The accuracy of Broman's method for supravital analysis of the barrier was confirmed in our group IV cats in which the barrier was found to be disrupted at 9° C. or less using either supravital or intravital methods.

REFERENCES

1. Bakay, L. *The Blood-brain Barrier, with Special Regard to the Use of Radioactive Isotopes.* Charles C Thomas, Springfield, 1956.
2. Broman, T. Supravital analysis of disorders in the cerebral vascular permeability in man. Acta med. scandinav., **118:** 79–84, 1944.
3. Broman, T. Supravital analysis of disorders in the cerebrovascular permeability. III. A critical analysis of the technique and results obtained in experimental animals. Acta psychiat. et neurol., **25:** 19–31, 1950.
4. Broman, T. On basic aspects of the blood-brain barrier. Acta psychiat. et neurol., **30:** 116–124, 1955.
5. Broman, T. and Olsson, O. The tolerance of cerebral blood vessels to a contrast medium of the diodrast group. An experimental study of the blood-brain barrier. Acta radiol. Stockh., **30:** 326–342, 1948.
6. Caranna, L., Montgomery, V. and Swan, H. Lowering of the mean terminal temperature of surface-cooled dog by intravenous heparin. 45th Annual Clinical Congress of the American College of Surgeons, 1959.
7. Clemedson, C., Hartelius, H. and Holmberg, G. Effect of carbon dioxide inhalation on the blood-brain barrier. Nature, London, **178:** 915, 1956.
8. Friedemann, N. Blood-brain barrier. Physiol. Rev., **22:** 125–145, 1942.
9. Fukuda, T. A re-evaluation of the intra-arterial methylene blue (method of Ehrlich) in studies of the central nervous system. Arch. für Japanische Chirg., **26:** 507–514, 1957.
10. Goldmann, E. E. In: Arch. f. klin. Chir., **101:** 735–741, 1913.
11. Grontöft, O. Intracranial hemorrhage and blood-brain barrier problems in the newborn. Acta pathol. et microbiol. scandinav., Suppl. C, 1954.
12. King, L. S. The hematoencephalic barrier. Arch. Neurol. and Psychiat., **41:** 51–72, 1939.
13. Klatzo, I., Piraux, A. and Laskowski, E. J. The relationship between edema, blood-brain barrier and tissue elements in a local brain injury. J. Neuropath. and Exper. Neurol., **17:** 548–564, 1958.
14. Laskowski, E. J. Observations on the effects

of hypothermia on experimental brain lesions. Surgical Forum of the Amer. College of Surgeons, p. 714, 1958.

15. Lee, J. C. and Olzewski, J. Effect of air embolism on permeability of cerebral blood vessels. Neurology, **9:** 619–625, 1959.
16. Lougheed, W. M. and Kahn, D. S. Circumvention of anoxia during arrest of cerebral circulation for intracranial surgery. J. Neurosurg., **12:** 226–239, 1955.
17. Macklin, C. A. and Macklin, M. T. A study of brain repair in the rat by use of trypan blue, with special references to the vital staining and the macrophages. Arch. Neurol. & Psychiat., **3:** 353–394, 1920.
18. Rodriquez, L. A. Experiments on the histologic locus of the hemato-encephalic barrier. J. Comp. Neurol., **102:** 27–45, 1955.
19. Rosomoff, H. L. and Gilbert, R. Brain volume and cerebrospinal fluid pressure during hypothermia. Am. J. Physiol., **183:** 19–22, 1955.
20. Stone, H. H., Donnelly, C. and Frobese, A. S. Effect of lowered body temperature on cerebral hemodynamics and metabolism of man. Surg., Gyn. & Obst., **103:** 313–317, 1956.
21. Tschirgi, R. D. Blood-brain barrier. In: *The Biology of Mental Health and Disease*, pp. 36–46. Hoeber, New York, 1952.
22. Wislocki, G. B. and Leduc, E. H. Vital staining of the hematoencephalic barrier by silver nitrate and trypan blue, and cytological comparison of the neurohypophysis, pineal body, area postrema, intercolumnar and supra-optic crest. J. comp. Neurol., **96:** 371–414, 1952.
23. Woodhall, B., Reynolds, D. H., Mahaley, S., Jr. and Sanders, A. P. The physiologic and pathologic effects of localized cerebra hypothermia. Ann. Surg., **147:** 673–683, 1958

MACH AND PSYCHOANALYSIS[1]

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INTRODUCTION

The name of Ernst Mach is familiar to all students of science and human thought. Yet, probably relatively few persons nowadays study his original writings. Perhaps in part this is due to the fact that English translations of his works have been out of print for some years and therefore are not readily available.[3] If so, the re-issue of Mach's *The Analysis of Sensations* (21) should be of interest to a wide circle of readers. Its relevance today, of course, is principally historical. This, however, should not be construed to mean that Mach's views are outdated—although, in a sense, they are—for no serious student of any branch of science can afford to remain ignorant of the historical antecedents of his present ideas.

Although Mach officially was a physicist, he wrote the present work as a contribution, at least in part, to psychology. The scope and method of this field of knowledge he conceived on the model of Fechner's *Psychophysics*. In terms of present-day divisions of science, this book is relevant to the following areas or topics: physics and its philosophy; psychology, including therein psychoanalysis; psychosomatic medicine or the problem of "correlations" between psychological and physical processes or statements; and, finally, epistemology and the philosophy of science. Mach's important influence on the development of physical thought has been discussed by several workers (4, 11, 22). For this reason, and also because I am not qualified to discuss this subject, I shall make no further comments on this aspect of Mach's work. My aim in this essay shall be first to sketch the historical and social scene of Mach's time, and then to comment briefly on Mach's role in the development of the philosophy of science. Finally, I shall discuss in detail the connections, historical as well as conceptual, between some of Mach's ideas and the origin of psychoanalysis.

MACH AND HIS TIME

Ernst Mach was born in 1838, in Turas, Moravia, then a part of the Austro-Hungarian Empire. He was ten years old in 1848, when, in the wake of the spirit of liberalism that swept eastward from France, the Hungarian revolution against the Hapsburg Monarchy erupted. Although the revolution as a movement for national independence failed, it signaled the beginning of a slow process of democratization in Austria-Hungary. In the course of this, serfdom was abolished and increasing recognition was given to the linguistic identity and self-determination of the various national groups (such as Czech, Slovak, Hungarian, Rumanian and Serbian) which composed this major European power. Parallel with these political and social changes, an atmosphere developed which was very encouraging to the growth of the arts and sciences. To Vienna, which was already a significant European cultural center, were added the capital cities of Budapest and Prague as centers of rapidly developing industry, commerce, science and art. The years between 1848 and the first World War in Austria-Hungary were characterized by a widespread belief in the stability and security of the government and the State, coupled with a belief that forces promoting slow but steady changes toward

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[3] A new printing of Mach's *Principles of Physical Optics* is also available (19).

ever better social conditions were constantly at work. This, at least, was the social *Weltanschauung* of the middle, upper and still higher classes of this society. Almost all of Mach's life (he died in 1916) was spent during this epoch which could be called the "Age of Security" (in Central Europe). Freud, too, and of course many other outstandingly creative personalities, lived and produced much of their life work during this period.

It should also be remembered that although Austria-Hungary was officially a Roman Catholic country—atheism being outlawed much as abortion is outlawed in this country at present—the romantic enthusiasm for knowledge and science made people oblivious to the potential conflicts between the free pursuit of research and the interests of any given social or political group. The spirit of the times, I believe, could be characterized as one of romantic rationalism. It was widely felt that the growth of "knowledge"—perhaps visualized on the model of "love" and "charity"—could only serve the best interests of every one. These considerations merit emphasis partly because this social scene was probably instrumental in fostering the development of a certain kind of free and skeptical scientific spirit; and partly because of the significant differences between this cultural atmosphere and the social characteristics of the dominant contemporary cultures. Finally, these factors are relevant to an understanding of the scientist's attitude toward religion during the period in question. It should be noted in this connection that the general attitude toward religion tends to be more skeptical and lighthearted in a society in which it is imposed by governmental authority than it is in those countries in which it is encouraged but not enforced. While this matter is of no importance for Mach's work, it is for Freud's and is mentioned for that reason. Although Freud was much preoccupied with "fighting" religion (principally Roman Catholicism), he was also strongly influenced by it. He was, moreover, similarly influenced by the physicalistic world-view of contemporary science, a view which Freud accepted *in toto*, but which Mach questioned and challenged.

It is, of course, largely speculation to attempt to assess the relationship (if any) between the social scene which I have sketched and the development of thought-systems, such as positivism and psychoanalysis. The only common denominator of these two movements was the questioning of the foundations of traditional thought and belief in their respective domains. Mach doubted the "absolutes" implicit in the epistemology of Newtonian physics; and Freud challenged the belief that problems of human health and illness could be encompassed within the confines of traditional medicine. Can we entertain such, or similar, fundamental doubts concerning segments of our life-experiences unless we rest on firm footings in other—personal, social, etc.—areas? I think not. The value of the sociology of science, and of the psychology of the scientist, depends in large part on our ability to arrive at connections such as have been suggested above, and to demonstrate their validity.

MACH AND THE PHILOSOPHY OF SCIENCE

Mach is generally credited with initiating the systematic study of what has become known as the "philosophy of science." "Since the time of Ernst Mach," wrote von Mises, "natural scientists have known that the explanation or the theory of a group of phenomena is only a description of the facts on a higher level" (22, p. 8).

Until the turn of the century—and in some of the non-physical sciences even today—it was thought that the proper aim of science was to produce "objective descriptions" of nature and to formulate these economically by theories which are "true." Mach challenged this illusory security of "science" and "truth" which was associated with Newtonian physics (18). In doing so, he

stirred up a revolution in man's thought regarding himself and his place in nature. For it had been assumed that the *security* of theological dogma—which was rapidly losing credence—would be replaced by a new source of *certainty*, namely, that found in "scientific truth." The attack on this conception of science was initiated by Mach. His "relativistic" conception of the task and nature of science was subsequently supported and vastly expanded by Einstein, Russell and a galaxy of mathematicians, physicists and philosophers (1, 2, 25, 35). Thus, the last half-century not only has been a time for the rapid development of physical science and technology, and of psychoanalysis and the social sciences, but also—and of equal significance—for the development of logical positivism, modern empiricism and operationalism. These three are the principal "schools" of modern philosophical thought whose concern is the "science of science."

Mach's role in the development of the philosophy of science has been expertly presented by Philipp Frank (10, 11) and Richard von Mises (22). The interested reader will profit from these works. Frank also commented on what may be regarded as the spiritual or psychological implications of Mach's view (and of the modern scientific view) on the nature of science, particularly in relation to the problem of truth and certitude. His appraisal of this important sociopsychological feature of science in the abstract, and concretely of what scientists do, is worth quoting in full:

> "It is not to be denied that the philosophy of enlightenment possesses a tragic feature. It destroys the old systems of concepts, but while it is constructing a new system, it is also already laying the foundations for new misuse. For there is no theory without auxiliary concepts, and every such concept is necessarily misused in the course of time. The progress of science takes place in eternal circles. The creative forces must of necessity create perishable buds. They are destroyed in the human consciousness by forces which are themselves marked for destruction. And yet, it is this restless spirit of enlightenment that keeps science from petrifying into a new scholasticism. If physics is to become a church, Mach cries out, I would rather not be called a physicist. And with a paradoxical turn, Nietzsche comes out in defense of the cause of enlightenment against the self-satisfied possessor of an enduring truth:
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> 'The assertion that the truth is here, and that an end has been made of ignorance and error, is one of the greatest seductions that there are. Assuming that one believes it, then the will to test, investigate, predict, experiment, is crippled: the latter can itself become wanton, can doubt the truth. The "truth" is consequently more ominous than error and ignorance because it binds the forces with which one can work for enlightenment and knowledge.'
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> Of these forces, however, at the turn of the century, Mach was one of the mightiest" (10, p. 78).

The tentativeness inherent in this picture of the scientific attitude (33) has the greatest importance for psychology, for it is the task of psychology, as one of the sciences concerned with man's behavior, to contribute to our understanding of the factors which make such an attitude possible. Today, we have only the faintest glimmers of some of the things which happen to people that make it possible for them to temper, to withstand and to outgrow what seems to be the child's basic need for certainty, and its corollaries, trust and belief. The scientific attitude implies a well developed capacity to tolerate uncertainty and skepticism—at least toward some segments of one's life experiences—and their corollaries, the wish to explore and test, and the integrity to doubt constructively. Mach possessed these psychological capacities to an exceptionally high degree. In *The Analysis of Sensations*, for instance, he could say that "No point of view has absolute, permanent

validity. Each has importance only for some given end" (21, p. 37).

Mach, moreover, could not *only* say this but could implement his views by solid scientific accomplishments embodying his principles.

This is not the place to discuss or evaluate Mach's scientific achievements. In this regard, it should suffice for our purpose to cite (from Frank) parts of Einstein's obituary notice on Mach, published in the *Physikalische Zeitschrift* in 1916:

> "Concepts have meaning only if we can point to objects to which they refer and to the rules by which they are assigned to these objects. He (Mach) conceived every science as the task of bringing order into the elementary single observations which he described as 'sensations.' This denotation was probably responsible for the fact that this sober and cautious thinker was called a philosophical idealist or solipsist by people who had not studied his work thoroughly. . . . I can say with certainty that the study of Mach and Hume has been directly and indirectly a great help in my work. . . . Mach recognized the weak spots of classical mechanics and was not very far from requiring a general theory of relativity half a century ago. . . . It is not improbable that Mach would have discovered the theory of relativity, if, at the time when his mind was still young and susceptible, the problem of the the constancy of the speed of light had been discussed among physicists" (9, pp. 271–272).

The latter remark may be thought to be rather generous, as was suggested by Popper (24). However that may be, it seems unlikely that Einstein would have bestowed such praise on many other contemporary physicists. In his "Autobiographical Notes," Einstein had this to say concerning Mach's influence on his thinking:

> "We must not be surprised, therefore, that, so to speak, all physicists of the last century saw in classical mechanics, a firm and final foundation for all physics, yes, indeed, for all natural science, and that they never grew tired in their attempts to base Maxwell's theory of electromagnetism, which, in the meantime, was slowly beginning to win out, upon mechanics as well. Even Maxwell and H. Hertz, who in retrospect, appear as those who demolished the faith in mechanics as the final basis of all physical thinking, in their conscious thinking adhered throughout to mechanics as the secured basis of physics. It was Ernst Mach, who, in his *History of Mechanics*, shook this dogmatic faith; this book exercised a profound influence upon me in this regard while I was a student. I see Mach's greatness in his incorruptible skepticism and independence; in my younger years, however, Mach's epistemological position also influenced me very greatly, a position which today appears to me to be essentially untenable" (7, p. 21).

These remarks are interesting, not only because they contain a brief summary of the evolution of physical thinking from classical Newtonian mechanics to relativistic mechanics, but also because what Einstein called "the faith in mechanics as the final basis of all physical thinking" has been applied, so to speak, to the foundations of psychoanalysis as well (5, 27). I shall discuss this in the next section of this paper.

Before concluding this brief commentary on Mach's role in the philosophy of science, it may be well to note that he used the word "sensation" in a sense that is quite different from its current use in psychology (6, 29). Indeed, Mach himself was aware of his somewhat peculiar use of this word and called attention to it in the following passage:

> "In what follows, wherever the reader finds the terms 'sensation,' 'sensation-complex,' used alongside of or instead of the expressions 'element,' 'complex of elements,' it must be borne in mind that it is *only* in the connexion and relation in

question, *only* in their functional dependence, that the elements are sensations. In another functional relation they are at the same time physical objects. We only use the additional term 'sensations' to describe the elements, because most people are much more familiar with the elements in question as sensations (colors, sounds, pressures, spaces, times, etc.), while according to the popular conception it is particles of mass that are considered as physical elements, to which the elements, in the sense here used, are attached as 'properties' or 'effects.' In this way, accordingly, we do not find the gap between bodies and sensations above described, between what is without and what is within, between the material world and the spiritual world" (21, pp. 16–17).

In other words, Mach's "sensations" are much closer to what we (also) call "physical objects" than we might assume on the basis of the common use of this word. This usage explains, too, why Mach spoke of "sensations" of space and time. Yet, in so doing he did not differentiate between those *aspects* of what we would today call "time experience" which are shared and public and are therefore studied by the methods of physics —and those which are unshared, private, and dependent on personal-historical and bodily factors, and are accordingly best studied by the methods of psychology (25). For this, Mach and his philosophical ideas have been subjected to scathing criticism by many workers. In the *Encyclopaedia Britannica*, for instance, Mach's work is dismissed with a curt note, ending with this reproach: "His whole theory appears to be vitiated by the confusion of physics and psychology" (8, p. 574). This sweeping condemnation of Mach's philosophical position seems to me completely unjustified. It appears to rest on an unrealistic expectation—in the light of Mach's historical position—concerning his ideas on the relation of physics to psychology. As to the "sin" of confusing physics and psychology, I believe that this is still rampant among us, but is nowadays often disguised as "physiological psychology" or as "psychosomatic medicine" (30, 31, 34).

MACH AND PSYCHOANALYSIS

The connections, if any, between Mach and Freud, and their respective works, have thus far not received attention. Judging from Jones' monumental biography of Freud, it can be assumed that there was no personal contact of any kind between the two men (16). It appears, however, that there may have been some very significant connections between Mach and Freud, even if these were not based on a personal relationship.

To begin with, Mach (1838–1916) was a contemporary of Joseph Breuer (1842–1925). Mach was thus 18 years older than Freud, who in turn outlived him by 23 years. Mach made numerous references to Breuer's researches (17, 20, 21). In particular, he was interested in Breuer's work on the physiology of the inner ear and the mechanisms of hearing and equilibration. In *Space and Geometry* (20), for instance, Mach referred to a paper which Breuer read to the Gesellschaft der Ärzte, in Vienna, in 1873. (Freud was then 17 years old.) And when, in 1894, Breuer was elected a Corresponding Member of the Vienna Academy of Sciences, one of his proposers was Mach (16, Vol. I, p. 122). It may be surmised, therefore, that Mach and Breuer were personally acquainted and perhaps on friendly terms. This, however, is merely an assumption on my part, for I have no information other than what has been mentioned concerning the relationship between them.

In all of Freud's writings, and in all of of the extensive Freudiana that has been published, I encountered, so far as I can recall, only one *significant* reference to Mach. It is in a letter to his friend, Wilhelm Fliess, dated June 12, 1900. In it, Freud wrote:

> "Do you suppose that some day a marble tablet will be placed on the house, inscribed with these words: 'In this house

on July 24th, 1895, the Secret of Dreams was revealed to Dr. Sigmund Freud.'

At this moment, I see little prospect of it. But when I read the latest psychological books (Mach's *Analyse der Empfindungen*, second edition, Kroell's *Aufbau der Seele*, etc.) all of which have the same kind of aims as my work, and see what they have to say about dreams, I am as delighted as the dwarf in the fairy tale because 'the princess doesn't know' " (13, p. 322).

A number of interesting points might be noted in connection with this statement of Freud's. Mach, at this time, was a full Professor in the University of Vienna. He already had achieved world-reknown as a physicist and philosopher. Yet, Freud referred to him here *as if* he were a psychologist and an expert on dreams. Surely, it is true that *The Analysis of Sensations* does not contain anything of value concerning dream-psychology. Nor was it addressed to this topic. Freud, as we know, had much coveted the social recognition which a regular professorship at the outstanding University of Vienna implied. This desire and his conflicting attitudes about it may have influenced him in two ways. On the one hand, he selected—presumably not without reason—Mach's somewhat unrelated work with which to compare what he felt was his *magnum opus. The Interpretation of Dreams*, it must be remembered, was also his first psychological book written alone.[4] He thus compared his work—in his own mind and to his friend—with that of the well-recognized University professor, Mach, in order to prove its originality and worth. On the other hand, however, I believe he was also much influenced by the general *epistemological outlook* inherent in Mach's psychological writings. This, particularly as it involved his views concerning the relationship between physics (medicine) and psychology, Freud borrowed from Mach. Indeed, perhaps Mach's prestige and authority may have even handicapped Freud, and the other founders of the science of psychoanalysis, from fully realizing the physicalistic basis upon which they have placed psychoanalysis.[5]

In his biography of Freud, Jones made a reference to Mach which, while not significant, is of some interest in this connection. It is in one of his letters to Freud (written in 1925), in which he wrote as follows:

> "At a recent dinner of the Anglo-Austrian Society at which I was present, Lord Haldane, the guest of the evening, dealt in his speech with the contributions made to culture throughout the ages by Vienna. The four names he singled out to illustrate this were Mozart, Beethoven, Mach and Freud" (16, Vol. III, pp. 109–110).

Returning now to the physical basis of psychoanalysis, I shall quote some excerpts from *The Analysis of Sensations* in order to display the close correspondence between Mach's and Freud's views concerning the nature of psychology as a science, and its relation to physics (physiology).

> "We may thus establish a guiding principle for the investigation of sensations. This may be termed *the principle of the complete parallelism of the psychical and physical*. According to our fundamental conception, which recognized no gulf between the two provinces (the psychical and the physical), this principle is almost a matter of course; but we may also enunciate it, as I did years ago, without the help of this fundamental conception, as a heuristic principle of research" (p. 60).[6]

[4] Freud's first book, *Aphasia*, published in 1891, was a neurological work. It was dedicated to Breuer (16, Vol. 1, pp. 212–213).

[5] I have discussed this subject in greater detail elsewhere (27–30).

[6] Fifty-four years after Mach first enunciated this principle, it was restated as the philosophical position of the Editors of the newly founded journal, Psychosomatic Medicine. In an "Introductory Statement," it was stated, "Emphasis is put on the thesis that there is no logical distinction between 'mind and body,' mental and physical. It is assumed that the complex neurophysiology of mood, instinct, and intellect differs from other

And toward the end of the book, Mach wrote:

"Thus, although *my ideal of psychology* is that it should be purely *physiological*, I should nevertheless think it a great mistake to reject so-called 'introspective' psychology entirely. For self-observation is not only an important means, but in many cases is the only means of obtaining information as to fundamental facts" (italics added, p. 340).

"The science of psychology is *auxiliary* to physics. The two mutually support one another, and it is only when they are united that a complete science is formed" (p. 341).

Addressing himself to the same problem, namely to the nature of the scientific status and role of psychology, James Strachey, the Editor and most recent translator of Breuer and Freud's *Studies on Hysteria*, wrote:

"Apart from the influence of Charcot, on which Freud never ceased insisting, it must be remembered, too, that both Breuer and Freud owed a fundamental allegiance to the school of Helmholz, of which their teacher, Ernst Brücke, was a prominent member. Much of the underlying theory in the *Studies on Hysteria* is derived from the doctrine of that school that all natural phenomena are ultimately explicable in terms of physical and chemical forces" (3, p. xxii).

It should be recalled, also, that the "school of Helmholz" (broadly understood) was continued and strengthened not only by Ernst Brücke but also by Mach himself. The psychophysical parallelism inherent in the thinking of all these workers rested most heavily on Theodor Fechner's "psychophysics." The degree to which physics (physiology, medicine) and psychology (including what we now call psychiatry and psychotherapy) were combined in those days is best illustrated by the fact that the outstanding scientists with whose names we are concerned here all combined two or more of these scientific roles (31). Thus, Helmholz was a physician, psychologist-physiologist, *and* experimental physicist, Breuer a physician, physiologist *and* psychotherapist, Fechner and Mach physicists *and* psychologists, and Freud physician (neurologist) and psychologist.

Considerations of the sociology of the scientific era in which Freud grew up, developed and worked furnish the necessary information for our understanding of his views concerning the "physical basis" for all "medical" (including psychological) problems.[7] Inasmuch as Mach was one of the leading physicists and philosophers of this era, his views on psychology and its relationship to physics are of the greatest importance for the student of the history of science in general, and of contemporary psychology in particular. The significance of this historical perspective on the epistemological foundations of psychology is enhanced by the fact that Mach's and Freud's bias in favor of the supremacy of the physical sciences has continued to flourish up to the present time. The extent to which Freud contributed to the persistence of this physicalistic bias in psychoanalysis is difficult to assess. That he laid the groundwork, however, for such an epistemology can not be doubted, as the following quotations show.

In the Editor's Introduction to *Studies on Hysteria* (quoted earlier), we read that:

"To the end of his life, however, Freud continued to adhere to the chemical aetiology of the 'actual' neuroses and to believe that a *physical basis for all mental phenomena* might ultimately be found" (italics added, 3, p. xxiv).

physiology in degree of complexity but not in quality" (14, p. 4).

[7] The following comments must not be regarded as giving a balanced presentation of Freud's position on this issue. His personality, as well as his work, was complex, many-sided, and at times, self-contradictory. Because of the scope of this essay, I have discussed only Freud's interest in the physicalistic basis of psychology. The weight of his work, however, argues powerfully for a genuine and epistemologically independent science of man as social being (23).

Freud stated this view repeatedly and in various ways. Perhaps the most significant formulation of his position concerning this matter is to be found in his "Postscript" to a "Fragment of An Analysis of a Case of Hysteria," published in 1905. He wrote:

> "Some of my medical colleagues have looked upon my theory of hysteria as a purely psychological one, and have for that reason pronounced it *ipso facto* incapable of solving a pathological problem. They may perhaps discover from this paper that their objection was based upon their having unjustifiably transferred what is a characteristic of the technique on to the theory itself. It is the therapeutic technique alone that is purely psychological; the theory does not by any means fail to point out that neuroses have an organic basis—though it is true that it does not look for that basis in any pathological-anatomical changes, and provisionally substitutes the conception of organic functions for the chemical changes which we should expect to find but which we are at present unable to apprehend. No one, probably, will be inclined to deny the sexual function the character of an organic factor, and it is the sexual function that I look upon as the foundation of hysteria and of the psychoneuroses in general. No theory of sexual life will, I suspect, be able to avoid assuming the existence of some definite sexual substances having an excitant action. Indeed, of all the clinical pictures which we meet with in clinical medicine, it is the phenomena of intoxication and abstinence in connection with the use of certain chronic poisons that most closely resemble the genuine psychoneuroses" (12, p. 113).

This quotation speaks for itself. It is an *apology* for the psychological nature of psychoanalysis and, as such, was destined to invite the fateful consequences of all excuses, in accordance with the psychological law expressed by the French saying, "Qui s'excuse, s'accuse!" The exact extent of the injury which this apologetic attitude has inflicted on medical psychology (including psychoanalysis) is, of course, difficult to estimate. But I would venture to suggest that the damage done has been considerable and persistent.

While for the contemporary reader the principal interest of *The Analysis of Sensations* lies, I believe, in its relevance to the philosophical foundations of psychoanalysis, this work also contains observations which merit attention and interest by virtue of their factual or theoretical importance. I shall call attention to only two of these.

Mach anticipated many psychologists and philosophers in making the following significant statement about "deceptions and illusions:"

> "The expression 'sense-illusion' proves that we are not yet fully conscious, or at least have not yet deemed it necessary to incorporate the fact into our ordinary language, *that the senses represent things neither wrongly nor correctly.* All that can be truly said of the sense-organs is, that, *under different circumstances they produce different sensations and perceptions.* As these 'circumstances,' now, are extremely various in character, being partly external (inherent in the objects), partly internal (inherent in the sensory organs), and partly interior (having their activity in the central organs), it can sometimes appear, when we only notice the external circumstances as if the organ acted differently under the same conditions. And it is customary to call the unusual effects, deceptions or illusions" (21, p. 10).

The psychoanalytic notion of "reality-testing" formulates man's acquaintance with his environment in radically different terms; it has recodified the time-honored (but misleading) psychiatric notions of hallucination and delusion (29). It is interesting to note, too, that Mach's important observations have been rediscovered, apparently independently, by several subsequent workers. William James, for instance, had this to say

on the subject (some forty years after Mach's above-mentioned article):

> "Sensations are forced upon us, coming we know not whence. Over their nature, order and quantity, we have as good as no control. *They* are neither true nor false; they simply *are*. It is only what we say about them, only the names we give them, our theories of their source and nature and remote relations, that may be true or not" (15, p. 160).[8]

And another forty years later, Gilbert Ryle cautioned that:

> "It is as absurd to call a sensation 'veridical' as to call it 'mistaken.' The senses are neither honest nor deceitful" (26, p. 237).

Finally, for the psychoanalyst perhaps the most interesting bit of psychological insight on Mach's part is his anticipation of the fundamental concept of transference. He wrote:

> "When once the inquiring intellect has formed, through adaptation, the habit of connecting two things, A and B, in thought, it tries to retain this habit as far as possible, even where the circumstances are slightly altered. Wherever A appears, B is added in thought. The principle thus expressed, which has its root in an effort for economy, and is particularly noticeable in the work of the great investigators, may be termed the *principle of continuity*" (21, p. 57).

Here Mach anticipated a basic idea of *learning theory*. This "principle of continuity" was named "conditioning" by Pavlov and was developed into an elaborate system of experimental psychology and learning theory. The same idea finds expression in Freud's concept of "transference." In this concept, it was given the refinement and sophistication which it required before it could have become a useful theoretical construct in the realm of human psychology.

In this brief discussion of some of the possible connections between Mach and psychoanalysis, I have sought to call attention to certain historical and social antecedents of our present psychoanalytic views. If some of our present views are erroneous or misleading, it is for us—by "us" meaning all those who have followed in the footsteps of the early pioneers—to make the necessary corrections. This probably can be done only if one keeps in mind precisely what it is that is to be clarified, and how the nature of this very objective may have changed with the passage of time (32). I can illustrate this contention by citing another passage from Mach, showing how our conception and definition of what constitutes psychology has itself changed. Mach wrote:

> "Thus the great gulf between physical and psychological research persists only when we acquiesce in our habitual stereotyped conceptions. A color is a physical object as soon as we consider its dependence, for instance, upon its luminous source, upon other colors, upon temperatures, upon spaces, and so forth. When we consider, however, its dependence upon the retina (the elements K L M . . .), it is a psychological object, a sensation. Not the subject-matter, but the direction of our investigation, is different in the two domains" (21, p. 17).

Psychology, according to Mach's view, is what we would now consider to be the domain of the psycho-physiology of the special sense organs (investigated by workers in neuroanatomy, neurophysiology, clinical neurology, physiological psychology, etc.). Yet, today, we use the word "psychology" to denote principally the study of human experience and human relationships. If we are to be successful in our endeavors in this field, we shall probably have to pay more attention to the epistemological bases of our theories—and their historical roots—than has been our custom heretofore.

[8] James was personally acquainted with Mach, having visited him in Prague in 1882 (10, p. 79).

REFERENCES

1. Ayer, A. J. *Language, Truth and Logic*. Dover Publications, New York, 1952.

2. Braithwaite, R. B. *Scientific Explanation. A Study of the Function of Theory, Probability and Law in Science*. The University Press, Cambridge, 1955.
3. Breuer, J. and Freud, S. Studies on hysteria (1893–95). In *The Standard Edition of the Complete Psychological Works of Sigmund Freud*, Vol. 2. Hogarth Press, London, 1955.
4. Cohen, R. S. Hertz' philosophy of science: An introductory essay. In Hertz, H. *The Principles of Mechanics, Presented in a New Form*. Dover Publications, New York, 1956.
5. Colby, K. M. *Energy and Structure in Psychoanalysis*. Ronald Press, New York, 1955.
6. Drever, J. *A Dictionary of Psychology*. Penguin Books, London, 1952.
7. Einstein, A. Autobiographical notes. *Albert Einstein, Philosopher-Scientist*, Schilpp, P. A., ed., pp. 1–95. Tudor, New York, 1951.
8. *Encyclopaedia Britannica*, Vol. **14:** p. 574. Encyclopaedia Britannica, Chicago, 1949.
9. Frank, P. Einstein, Mach and logical positivism. In *Albert Einstein, Philosopher-Scientist*, Schilpp, P. A., ed., pp. 269–286. Tudor, New York, 1951.
10. Frank, P. *Modern Science and Its Philosophy*. George Braziller, New York, 1955.
11. Frank, P. *Philosophy of Science. The Link Between Science and Philosophy*. Prentice-Hall, Englewood Cliffs, N. J., 1957.
12. Freud, S. Fragment of an analysis of a case of hysteria (1905). In *The Standard Edition of the Complete Psychological Works of Sigmund Freud*, Vol. 7, pp. 1–22. Hogarth Press, London, 1953.
13. Freud, S. *The Origins of Psycho-Analysis; Letters to Wilhelm Fliess, Drafts and Notes, 1887–1902*. Basic Books, New York, 1954.
14. Introductory Statement. Psychosom. Med., **1:** 3–5, 1939.
15. James, W. *Pragmatism and Four Essays from the Meaning of Truth (1907–1909)*. Meridian Books, New York, 1955.
16. Jones, E. *The Life and Work of Sigmund Freud*, Vols. 1–3. Basic Books, New York, 1953–1957.
17. Mach, E. *Grundlinien der Lehre von den Bewegungsempfindungen*. Engelmann, Leipzig, 1875.
18. Mach, E. Newton's views of time, space, and motion. In *Readings in the Philosophy of Science*, Feigl, H. and Brodbeck, M., eds., pp. 165–170. Appleton-Century-Crofts, New York, 1955.
19. Mach, E. *Principles of Physical Optics*. Dover Publications, New York, 1954.
20. Mach, E. *Space and Geometry, in the Light of Physiological, Psychological and Physical Inquiry*. The Open Court Publishing Co., Chicago, 1906.
21. Mach, E. *The Analysis of Sensations, and The Relation of the Physical to the Psychical (1885)*. Dover Publications, New York, 1959.
22. Mises, R., von. *Positivism, A Study in Human Understanding*. George Braziller, New York, 1956.
23. Nelson, B., ed. *Freud and the 20th Century*. Meridian Books, New York, 1957.
24. Popper, K. R. A note on Berkeley as a precursor of Mach. Brit. J. Phil. Sc., **4:** 26–36, 1953.
25. Russell, B. *Human Knowledge: Its Scope and Limits*. Simon & Schuster, New York, 1948.
26. Ryle, G. *The Concept of Mind*. Hutchinson's University Press, London, 1956.
27. Szasz, T. S. A critical analysis of some aspects of the libido theory. The concepts of libidinal zones, aims and modes of gratification. Ann. New York Acad. Sc., **76:** 975–1009, 1959.
28. Szasz, T. S. Is the concept of entropy relevant to psychology and psychiatry? Psychiatry, **19:** 199–202, 1956.
29. Szasz, T. S. *Pain and Pleasure; A Study of Bodily Feelings*. Basic Books, New York, 1957.
30. Szasz, T. S. Psychoanalysis and medicine. In *Readings in Psychoanalytic Psychology*, Levitt, M., ed., pp. 355–374. Appleton-Century-Crofts, New York, 1959.
31. Szasz, T. S. Scientific method and social role in medicine and psychiatry. A. M. A. Arch. Int. Med., **101:** 228–238, 1958.
32. Szasz, T. S. The problem of psychiatric nosology. A contribution to a situational analysis of psychiatric operations. Am. J. Psychiat., **114:** 405–413, 1957.
33. Waddington, C. H. *The Scientific Attitude*. Penguin Books, West Drayton, Middlesex, 1948.
34. Woodger, J. H. *Biology and Language. An Introduction to the Methodology of the Biological Sciences including Medicine*. The University Press, Cambridge, 1952.
35. Young, J. Z. *Doubt and Certainty in Science*. Clarendon Press, Oxford, 1951.

PSYCHOLOGICAL STUDIES OF KORSAKOFF'S PSYCHOSIS: V. SPONTANEITY AND ACTIVITY RATE[1]

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Lack of initiative has been listed as a characteristic symptom of the Korsakoff syndrome from the earliest reports of the disease (1, 6, 9), alongside its defining attributes of loss of memory for recent events, incapacity for new learning, retroactive amnesia, disorientation and confabulation. A consistent association of amnesic symptoms with impaired spontaneity in a neurological disease is of considerable interest in view of Cobb's observation about mammals which had the cerebral cortex removed but the basal ganglia intact, that "all they seem to lack is initiative and spontaneity, as well as memory" (4, p. 71). It might thus seem possible that these two functions of the intact organism depend on one neural system, and that this is damaged in Korsakoff's psychosis. Russell's suggestion (13, p. 75) that patients recovering from concussion regain their memories by an effort of piecing them together, places the conative before the cognitive defect in one kind of amnesia. Many students of the Korsakoff syndrome have also stressed the primary significance of lack of initiative among its symptoms (*e.g.* 7, 12), and particularly those who like Bürger-Prinz (2, 3, 14) argue that its basic disturbance is at the "vital" rather than at the noetic level. Our experimental studies of the Korsakoff syndrome (*e.g.* 15), however, support Müller-Suur's (10) criticism of this view, and also agree with Freund and Srnec's (5) conclusion based on work with electric shock effects, that the amnesic symptoms are not entirely or even mainly the results of a diminished spontaneity.

This conclusion does not imply that the patients we have studied failed to display a marked lack of initiative. Admittedly, this symptom of the chronic phase of the Korsakoff syndrome did not always rise to prominence in interviews which tended to be sustained at a fairly high rate of activity by a constant flow of questions. But it could certainly not be missed when the patients were placed in social situations, *e.g.*, while assembled in groups of four, they were encouraged by the writer, who was sitting somewhat outside their circle, to start and to keep on talking about any matter that was of interest to them. Every time an attempt was made to form a discussion group from the twenty patients, in various combinations of membership, the experiment failed. The topics of the weather or the last meal were exhausted within a couple of minutes, and the group then subsided into silence with no apparent sign of discomfort. Individual members would always readily answer any question addressed to one or another, but themselves neither raised different topics, nor elaborated beyond the barest reply. Often enough the answer was an admission of ignorance or lack of interest, and no other member of the group would break the silence, unless expressly invited to. The one exception to this rule were the stock grievances of two patients, aired in and out of season, in stereotyped phrases.

This mood of passivity, however, did not extend to situations in which a task was clearly set to the patients. In a long series of laboratory experiments they proved to be most cooperative, not only responding readily but working away diligently at continu-

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ous tasks, and thus perhaps displaying the same lack of initiative by not stopping, as they did by failure to break into speech or action. While admitting their lack of spontaneity, one would be incorrect to infer from this a state of apathy which also implies low response rate and quick fatigue.

The present paper reports several experiments carried out with a view to testing the preceding observations about initiative and activity rate in chronic Korsakoff patients.

SUBJECTS

The Korsakoff patients studied have been described in detail in an earlier report (19). They all had a history of alcoholism, and had reached a fairly level phase of the disease at the time the experiments were conducted. These were carried out over a period of three years, during which the original group of 20 was reduced to 15 by the discharge of some and the transfer of other members. The age range of the larger group at the earlier date was 31 to 68 years (mean 52.9, *SD* 9.0). Control groups, matched for age, were provided by alcoholic patients who were either receiving psychotherapy at, or had been admitted to the Alcoholism Clinic of the Massachusetts General Hospital for treatment in the future. They came from much the same social setting as the Korsakoff patients, and like them had no alcohol in their systems at the time of testing. Unlike them, they were functioning with reasonable efficiency and were not known to suffer from any brain damage other than characteristic of the normal aging process.

METHODS AND RESULTS

Activity rate was tested by means of several verbal and motor tasks. Some of the former required a modicum of initiative, the others tested either latency of response to discrete instructions or rate of continuous activity. One of the continuous performance tasks, while testing activity rate, involved a more complex perceptual process than simple visual-motor co-ordination, and the first experiment here reported was not concerned with activity rate, but is relevant to the question of spontaneity.

Results were tested for significance by t ratio for mean differential scores within the same group, or for difference between mean scores of experimental and control groups; in the absence of homogeneity of variance Wilcoxon's (20) test for ranked data was used for inter-group comparison.

RESUMPTION OF UNCOMPLETED TASKS

The experiment, based on Ovsiankina's (11) classic study, set the subjects the task of solving a jigsaw puzzle, the assembly of a capital letter T cut out of wood 1 in. wide, $\frac{1}{8}$ in. thick, and so divided into four pieces that its reconstruction posed a very hard problem. The subjects were first shown the T properly assembled, and were asked to identify it. This they all did correctly in both experimental and control group. It was then explained to them that the letter would be broken up into its component pieces, and that their task was to reconstruct it. The pieces were jumbled up in the subject's view, and he was allowed four minutes to assemble them. Any time he did this incorrectly, he was told that the solution was wrong, and that he should go on trying. All but one of the 18 control subjects and every one of the 20 Korsakoff patients failed to reach a solution within four minutes. The pieces were then set aside but left on the table in front of the subject who was given three successive brief experimental tasks, none of which involved problem solving. These tasks lasted two to three minutes each, and were separated by intervals of two minutes. At the end of each of these tasks the experimenter said that he had to examine his records, and while he was busy the subject could rest or do as he wished. The experimenter then ostensibly immersed himself in his papers, but could in fact watch any activity that might be going on on the subject's table. A note was made of attempts to resume the interrupted puzzle. None of the subjects who

failed in the first trial period solved the problem subsequently, but all the controls made at least one attempt, 11 reverting to it on all three occasions; only a single Korsakoff patient resumed the task in one of the breaks, while the others did not try even once.

VERBAL TESTS

Rate of verbal production was examined by three different procedures:

1) Two tests of fluency were given; the one requiring the enumeration of as many different things one is likely to see in a street as the subject could list in 60 sec., the other asking the names of different animals with a time limit of 30 sec.

2) The completion, one by one, of the following six unfinished sentences: "A person is most helpless when ..."; "One's closest friends can be ..."; "A drunken man ..."; "People are praised when ..."; "A weak person does not often ..."; "A large crowd ..."

3) Word association. Three lists were used in this procedure, List A consisting of words which have no logical opposites, and B_1 or B_2 composed of words which do, *e.g. dry, pull, top*. The subject's initial instruction was to call out any word in response to those listed by the experimenter, as fast as he could think of one, "*e.g.* in answer to *black*, it could be *shoe* or *white* or *dark* or *color*." Lists A, and B_1 or B_2, alternating with subjects, were presented with this instruction. Then a new instruction was given, *i.e.*, to respond with the opposites of the words presented, and the remaining of the three lists was read out and immediately followed by a second presentation of the other B list. Each list consisted of ten words, but since it was arbitrarily decided that reaction times in excess of 10 sec. should not be scored, some substitute words were provided to replace those which would thus be excluded.

Several Korsakoff patients could think of no more than four things which can be seen in a street; the group mean was 8.8, the longest list given by one of its members 18. With a mean of 15.7, the control group named significantly more items, the t ratio being 4.20 ($p < .01$). The more specific directive to name animals increased the rate of fluency in both groups, but with a much greater effect on the Korsakoff patients. Their score for 30 sec. was 9.1 animals as compared with 5.6 things in the street; the mean difference ($t = 4.96$) was significant at the .01 level, while the corresponding test for the difference between the control group's two means, 10.3 and 12.5, did not yield a significant result ($t = 1.34$); neither was the difference between the two groups significant for animals named. A tendency to narrow the loose boundaries of the instruction was noticeable in several Korsakoff patients who listed various types of vehicles in succession, or in one who named twelve different kinds of stores, and another who followed up the mention of a store with an inventory of its contents, which was not credited to her score.

On the sentence completion test the Korsakoff patients' score of 23.8 sec. for the six sentences was slightly, though not significantly, below the controls' 25.0 sec.

The effect of a definite direction on the Korsakoff patients' speed of reaction appeared quite markedly in the word association test. Their mean association time (per word) was 3.08 sec. for list A and 2.44 sec. for list B; the corresponding scores of the control group were 2.52 and 2.49 sec. The differences between the mean scores of the groups were not statistically significant on any of the four lists but, while the directive to respond with opposites reduced the Korsakoff patients' association lag to 1.53 for the new and to 1.61 sec. for the familiar word list, that of the controls slightly increased to 2.56 for the new words, and was reduced by no more than .22 sec. with the repeated presentation of list B. For the Korsakoff group, the mean difference in speed of reaction to list B under the two instructions was significant with $t = 4.64$ ($p < .01$),

but so was the mean difference between their scores on list A and B under unrestricting instructions ($t = 3.18$, $p < .01$). Practice would hardly account for this difference; it is more likely that the mere possibility of following a directive, *i.e.*, to name opposites, helped to establish a set even though it was not explicitly stated. In the control group, the mean differences between reaction time under the two conditions of instruction or between lists A and B with unrestricted association were not statistically different.

MOTOR REACTION

Speed of simple and choice reaction, the former with an alerting signal as well as without, was tested by means of a lever response to light signals. The apparatus at the subject's end consisted of a box one ft. high and 5 in. wide, displaying in the vertical midline of the front panel three round lights, each one in. in diameter, with spaces of one in. between them. Starting from top, the three lights were red, yellow and green, and below them was the subject's response mechanism, a lever which could be depressed under very light pressure. The subject sat facing this box, leaning his dominant hand on the table so that one or several fingers rested on the lever. The experimenter controlled the switchboard opposite the subject at a distance of about four ft., and had an electric timer in front of him. Red, yellow, and green lights were each turned on by a different switch, and the first two were instantly extinguished by the flashing on of another light, the green by the subject's depression of the lever. The switch for the green light also started the electric timer, and the depression of the lever stopped its action. During one phase of the experiment a telegraph key was placed in easy reach of the subject's non-dominant hand, which on contact turned off the red light. Reaction time to red lights was not recorded. Incorrect response, *e.g.* pressure on the lever in response to a red, on the telegraph key in response to a green light, activated a silent light signal on the experimenter's switchboard.

The experiment consisted of three phases. The first tested *simple* reaction time, and consisted of 20 consecutive green light signals; the subject's instruction was to press the lever immediately on seeing the green light. The second phase was a test of *disjunctive* reaction; 20 green and 20 red signals were presented in a standard randomized order. The subject's instruction was to press the lever as soon as he saw the green light, the telegraph key as soon as he saw the red light flashing on. Third, *alerted*, *i.e.*, simple reaction following an alerting signal, was tested by a sequence of red-yellow-green lights. The subject was told that all three lights would be in operation, but that he should respond to the green light only, by pressing the lever as before. The entire series consisted of 100 sequences of light signals, of which the first eight and another 55 were the standard pattern of red-yellow-green (R Y G). The other patterns, spaced in standard positions within the series of 100, included 18 sequences of red-green (R G), nine of yellow-green (Y G), and ten red-yellow-red (R Y R). Since the lights had to be switched on separately, the duration of each varied within the limits empirically adopted by the experimenter. Except for R Y R signals, the subject's task was always the same, *i.e.* to push down the lever as soon as he saw the green light; but R G and Y G sequences reduced, and possibly confused, his alerting information. R Y R signals probed the interference effect of anticipatory sets by facilitating incorrect responses.

The results are set out in Table 1, and show that, faced with the simple reaction task, the Korsakoff patients differed from the controls neither in speed nor significantly in consistency of response. With a disjunctive instruction their reaction became significantly slower ($t = 5.07$) but the same happened in the control group as well ($t = 3.70$) and, though the latter lost less speed, the difference between the two groups is not

TABLE 1

Means of Reaction Time and Variances in .01 sec.

	Korsakoff N = 15	Control N = 15	*t* ratio	Wilcoxon's T
Mean reaction time				
Simple	37.5	37.4	0.02	
Disjunctive	53.8	48.6		203
Alerted				
R Y G	49.0	38.1	2.14*	
R G	60.2	48.0		175*
Y G	56.7	42.3	2.14*	
Mean variances				
Simple	240.0	122.8		200
Disjunctive	3377.0	118.6		148
Alerted: R Y G	136.5	59.5		198

* $p < .05$

TABLE 2

Continuous Motor Task: Counter Scores

	Mean score per 30 sec.		Mean variance of 10 periods		First minute–fifth minute	
	Right	Left	Right	Left	Right	Left
Korsakoff (N = 15)	88.2	79.7	118.8	108.1	9.5	17.9
Control (N = 15)	86.9	78.7	139.8	170.5	0.8	12.8

significant. In neither group did the full alerting signal make for the speediest responses. While the controls merely failed to benefit from it ($t = .24$), the Korsakoff patients reacted to it significantly more slowly than to the simple signal ($t = 3.45$); moreover, the mean difference between their disjunctive and alerted response was not statistically significant ($t = 1.71$). Partial alerting signals resulted in slower response in both groups, the delay being significantly larger for the Korsakoff patients. The differential effects of partial as against full alerting signals showed no significant differences between the two groups, neither did mean differential reaction times between disjunctive and simple or disjunctive and alerted response; the only exception was that between alerted and simple with T = 166 ($p < .01$). The control subjects were the more consistent in their reaction times, though significantly so only with the disjunctive task in which quite a few Korsakoff patients oscillated between extremely slow and fairly fast responses. Except for the simple reaction test, variability of reaction time across subjects was greater in the Korsakoff than in the control group. The few errors of incorrect response or failure to respond were about evenly divided between the two groups, and the bulk was contributed by two or three members in either.

WORK RATE

Two tasks probed the rate of continuous motor performance, one requiring some measure of manual skill. The two tasks were also performed in combination, in order to evaluate the effect of divided attention on the efficiency of the Korsakoff patients in continuous rather than alternative engagement. One task consisted simply of pressing down the lever of a counter for a period of five minutes, first with the thumb of the left hand, then for the same length of time with the right hand. The experimenter read the counter, while the subject continued to work it, at the end of each 30 sec. period. Variances were calculated for each subject's performance over the ten periods, and these, as well as means and decrement from the first to the fifth minute, provided the data summarized in Table 2.

The same work with the counter was performed on another occasion for two 60 sec. periods with the non-dominant hand only, forming part of a series of several tests, each of which lasted one minute. The first of these was that of moving small steel balls of ⅛ in. diameter from one bowl into another. The subject picked them up, one at a time, with a pair of tweezers held in his dominant hand, as fast as he could. The bowls were 3¾ in. wide on top, 3 in. at the bottom, and rested in sockets ¼ in. deep, their midpoints 6 in. apart. They were placed within comfortable reach, the one about one-third full to the right of right-handed subjects. A 60 sec. trial preceded the test. The second task consisted of pressing the lever of the counter;

TABLE 3

Single and Combined Manual Tasks: Mean Scores per 60 sec.

	Counter			Metal Balls		Blue Beads	
	Alone	With Metal Ball	With Blue Beads	Alone	With Counter	Alone	With Counter
Korsakoff (N = 16)	163.7	83.6	81.4	30.6	29.1	21.7	22.8
Control (N = 16)	182.5	124.6	122.1	32.0	27.7	27.3	26.6
t ratio	1.48	2.24*		0.32	0.41	1.84	1.30
Wilcoxon's T			206.5*				

* $p < .05$

the third of working the counter as before, and simultaneously picking up steel balls with the other hand. The fourth task differed from the first in presenting the subject with wooden beads of $^3/_{16}$ in. diameter instead of the steel balls. Blue and yellow beads were mixed in the bowl in equal numbers, and the task was to pick up only blue ones. The fifth test combined this task with lever pressing; and then all five were repeated in this order: 4, 5, 2, 3, 1. The scores, averaging counter readings and the number of beads correctly transferred under each of the five instructions, are set out in Table 3.

In pressing the counter, the difference between the mean scores of the two groups was very slight with either hand. The Korsakoff patients performed more steadily over the five minute period, but the difference between the mean variances of the two groups is not significant, neither is that between mean decrement from the first to the fifth minute. The two groups did not differ significantly in their performance on the other manual skill tasks, except that the Korsakoff patients were slower with the counter while engaged in moving beads. Divided attention resulted in a slower rate of counter pressing in both groups, while performance with the beads was unaffected. A further complication of the instruction, *i.e.*, to select blue balls only, significantly reduced the efficiency of the Korsakoff patients but not that of the control group. The *t* ratios for mean difference between metal balls and blue beads were 4.94 and 3.94 (both $p < .01$) for the Korsakoff group, 1.96 and .44 (both $p > .05$) for the control subjects.

REVERSAL

A task familiar from perseveration studies was used, in which subjects were instructed to write the letter *S* on a ruled page as many times as they could, first in the standard direction for 30 sec., then in reverse for 60 sec., and finally again in the standard direction for 30 sec. The test was preceded by a brief trial of writing *S*s in both directions. Mean scores of 20 Korsakoff patients for 60 sec. were 78.0 letters in standard direction, 35.3 in reverse; the corresponding means of 15 controls were 78.2 and 65.8 sec. The difference between the two groups in writing standard *S*s is not significant; the difference between mean differential scores (standard-reverse) is significant, with $t = 4.83$ ($p < .01$). The decrement of performance between the first and the final 30 sec. periods was slightly but not significantly larger in the experimental group (2.4 as against the control's 1.6), in accordance with their general tendency to reach their optimum level of performance rapidly, and to show little or no progress with practice.

CANCELLATION

Rate of performance, in an activity involving somewhat more complex selective processes than in those previously listed, was studied by means of a cancellation test. Three tasks were set to the subjects in succession, each consisting of five consecutive

TABLE 4

Cancellation: Mean Group Scores per 60 sec.

	Korsakoff	Control	*t* ratio	Wilcoxon's T
Correct cancellation: raw score				
Task A	26.3	49.8	5.24*	
Task B	29.4	52.4	5.11*	
Task C	30.9	54.5	5.02*	
Total error: raw score				
Task A	10.6	3.9		284.5*
Task B	20.5	4.6		253.5*
Task C	28.4	6.8		264*
Correct cancellation: ratio				
Task A	0.83	0.95		344
Task B	0.69	0.94		274.5*
Task C	0.64	0.83		257.5*
Error: ratio				
Task A	0.62	0.09		318.5
Task B	1.39	0.07		237*
Task C	1.53	0.15		254*

* $p < .01$

60 sec. work periods. The instruction for Task A was to cross out all capital letters found on a page on which letters were printed in unsystematic order, 40 to a line, 14 of which were capitals randomly distributed in each line. The work sheet of the other two tasks differed from the first in that the lines were interrupted by gaps of two spaces at irregular intervals, six to a line. The instruction for Task B was to "cross out every capital letter and every letter, whether large or small, which is preceded by a gap"; for Task C "to cross out every capital letter and every letter, small or large, which is just before or just after a gap." These instructions were printed on top of each page, followed by examples. Each task was preceded by some trials, and the test proper did not start until the subject clearly understood his instructions which, in some instances, took quite a little time and explanation. However, 20 Korsakoff patients managed to grasp the instructions and had sufficiently sharp eyesight to pass the trials, as did 20 control subjects. The following raw scores were obtained for each 60 sec. period on the three tasks: a) number of letters surveyed; b) correct cancellation; c) error by omission; d) error by incorrect cancellation. From these, further scores were derived, group means of which are set out in Table 4: mean correct cancellation per 60 sec.; total error (c plus d) per 60 sec; ratio of correct cancellation to letters to be cancelled; ratio of total error to correct cancellation, each listed separately for the three tasks.

In addition to the tabulated data the following points are worth noting. 1) Differential scores between task A on the one hand, tasks B and C on the other, were significant in the Korsakoff but not in the control group for correct cancellation, ratio of correct cancellation, and total errors. 2) Only in task A did the control group survey significantly more letters than the Korsakoff patients, the group means of capitals per 60 sec. being 52.4 and 31.9 and the *t* ratio 4.10 ($p < .01$). 3) Counting total cancellation, *i.e.* incorrect as well as correct, as a measure of activity rate, the control group performed significantly faster on each of the three tasks. 4) Neither group fluctuated much across the five 60 sec. periods, the Korsakoff patients' scores being at about the same level throughout, with just a slight tendency to make more errors by incorrect cancellation towards the end of each task; the controls very slightly increased their correct cancellation as they progressed with each of the three tasks. 5) In both groups, the higher a subject's ratio score was for correct cancellation, the lower tended to be his ratio score for errors, as shown by *rho* .76 for the Korsakoff patients, and .95 for the controls. 6) Of the two types of error, those by omission were the more numerous, forming 64, 78, and 83 per cent of the total error score in the Korsakoff group, 51, 77, and 83 per cent in the control group on the three tasks.

DISCUSSION

While confirming the clinical observations about the marked poverty of initiative in Korsakoff patients, the experiments have also shown that they perform simple tasks of

verbal response or manual skill as promptly and at much the same rate as the controls chosen for this study. There may be some doubt whether the latter formed a representative sample of their age group in the population at large; and more complex instructions clearly reveal certain defects characteristic of the Korsakoff syndrome. Before examining the criteria of complexity which distinguished the tasks in which the Korsakoff group proved less efficient than the controls, it should be stressed that neither these, nor success in the tests of spontaneity depended on intact memory. The pieces of the *T* were spread out in front of the subjects to remind them of their failure with the puzzle, and none of the other tasks was sufficiently protracted to let them forget their instructions.

Given a simple instruction, Korsakoff patients keep up their activity for a considerable time. By the evidence of the word fluency and word association tests, they perform more easily under closely defined directives than with relatively indeterminate instructions; while for the controls any facilitating effect of such a directive tended to be offset by a greater care about accuracy. The problem of accuracy did not arise with the loose instruction (*e.g.*, things in a street, unrestricted association) and did not appear to cause any concern to the Korsakoff patients when closer directives were given. The fact that, in spite of this, they responded correctly in almost every instance is remarkable, and serves as a reminder that their memory is not completely deranged. The contrast between the Korsakoff patients' efficient use of words and their failure to memorize events has often been remarked on. The patients studied in this research project never seemed to be at a loss for the right word or phrase, certainly not more so than highly verbal and healthy men and women, and, judged by the experiment in controlled association, used their vocabulary as efficiently as a control group which was free from amnesic symptoms. The sentence completion task points to much the same conclusion, though a qualitative analysis might have brought out the inferiority of the Korsakoff group's performance.

The word fluency test called for more initiative than the other verbal tasks, and was evaluated for quantity of output rather than for speed of response, since even 30 sec. was more than sufficient time to allow for those names which came immediately to the subject's mind. Nevertheless, the conclusion drawn from the verbal reaction tasks also emerges from the results of this test, *i.e.*, the more definitive the directive the less are the Korsakoff patients hampered by their disability. Clearly, the memory defect of these patients placed them at no greater disadvantage when listing things in a street than in enumerating species of animals; as a matter of fact, the amnesic symptoms of Korsakoff's psychosis should not be expected to come to the surface with either of these examples of early learning.

The motor tasks, of course, did not test the effect of diffuse direction on the performance of the Korsakoff patients, but explored various aspects of divided attention or set on immediate response and rate of performance. It appears that, at least in comparison with the control group of this study, the peripheral mechanisms involved in quick reaction and in continuous action are undamaged in the chronic phase of the Korsakoff syndrome; neither did performance fluctuate more, nor fatigue set in sooner. Even the comparatively fine skill required for picking up small beads appeared to be unimpaired, and the additional perceptual task of selecting beads of one color was discharged adequately, as was that of a disjunctive response. It should be pointed out though that all these observations are valid only for the specific damage of the Korsakoff syndrome, not for the total effect of those alcoholic habits which were common to experimental and control group in this study. Both groups were slower in simple and disjunctive reaction than would be expected,

by the evidence of our experiments, from their age group, but not less efficient in the other motor tests. Nevertheless, the findings are of interest in view of the severe peripheral neuritis characteristic of the early phase of the Korsakoff syndrome.

Any motor defects characteristic of Korsakoff's psychosis emerge only when attention has to be divided between two dissimilar tasks, both in rate of performance (counter and beads) and in steadiness of response (disjunctive reaction). Further decrement occurs when attention has to be turned to yet another, third, task, as in sorting out blue beads before picking them up, while working the counter. Alerting signals did not help to speed up the Korsakoff patients' simple reaction, in fact they slowed it down, a paradoxical effect observed in healthy older men and women as well. At the behavioral level, at any rate, these warnings, whether complete or partial, instead of releasing an inhibitory process tend to prolong it. This finding accords with other experimental evidence (16–18) of the poor flexibility Korsakoff patients show in changing sets, *e.g.* in tests of simple perception and problem solving. Further indication of this disability is furnished by the tests of writing *S*s and of cancellation, the one requiring the reversal of an old established orientation in performance, the other a constant shift of attention. The Korsakoff patients performed much less efficiently when their instruction for cancellation demanded a continuous alteration of set from one type of attribute (capital versus lower case type) to another (gap) which might occur jointly with the first but also might not. Admittedly, they differed significantly from the controls in correct cancellation and error on all three tasks, of which the first did not demand shifts in set. However, it did require continuous scanning, and that slowed down the Korsakoff patients' rate of performance; as a consequence, their ratio scores of correct cancellation and of error were not significantly different from those of the controls. Neither their accuracy nor their speed improved with practice, and generally they tended to reach the peak of their performance at an early stage of repetitive motor tasks.

While the findings here reported accord with other experimental results, as well as with some clinical observations made on the same group of patients, they differ from Hebb's (8) conclusion about the defects characteristic of non-aphasic deterioration following brain injury in adulthood, in that neither sentence completion nor the naming of opposites differentiated our Korsakoff patients from the controls. Let it be noted though that the qualitative criteria applied to these two tests were not very rigorous. On the other hand, the experiments support Hebb's findings concerning the negligible effect of such damage on the patient's vocabulary. Hebb's report, however, weakens any confirmation our Korsakoff group may have provided of Cobb's hypothesis quoted above, for one patient (H.D.) described by him combined inactivity and lack of initiative with good memory. The two defects are undoubtedly associated in the Korsakoff syndrome, but there is no evidence for regarding one as the secondary effect of the other. Korsakoff patients may indeed fail to recover lost memories for lack of effort in trying, but we have no ground for believing that any amount of effort would regain them. In the human organism these two broadly determined functions — spontaneity and memory—may be subserved by different neural systems, and possibly both these systems involve that area of the brain which is damaged in Korsakoff's psychosis.

SUMMARY

Some experiments have been reported which investigated spontaneity and activity rate in Korsakoff patients, both in immediate response and in continuous performance.

As compared with a control group of alcoholic patients, matched for age and without known brain damage, the Korsakoff pa-

tients showed no loss in speed of reaction on verbal or manual tasks, and their rate of continuous activity was also equal to that of the controls while engaged on a single task.

Korsakoff patients were slowed down in verbal tasks which failed to provide definite directives, on some manual skill tests which required a division of their attention between two or more tasks, and in activity which involved a reversal of old established habits or continuous scanning. Alerting signals failed to speed up their reaction, and in fact had the opposite effect. They did not spontaneously resume tasks interrupted before completion.

The results support several findings based on clinical observation and on experimental studies of Korsakoff patients. These patients lack initiative, and function most effectively under closely defined instructions. Their vocabulary is apparently intact and normally available. Their effector mechanisms show no impairment specific to the disease, and their poor retention of memories is not accompanied by low persistence or by a rapid abandonment of a set. On the contrary, their performance tends to be efficient as long as an old established or the first situationally induced set remains appropriate.

REFERENCES

1. Bonhoeffer, K. *Die akuten Geisteskrankheiten der Gewohnheitstrinker.* Fischer, Jena, 1901.
2. Bürger-Prinz, H. and Büssow, H. Über das amnestische Syndrom, Allg. Ztchr. Psychiat., **121:** 195–215, 1943.
3. Bürger-Prinz, H. and Kaila, M. Über die Struktur des amnestischen Symptomenkomplexes, Ztschr. Neurol. u. Psychiat., **124:** 553–595, 1930.
4. Cobb, S. *Foundations of Neuropsychiatry.* Williams & Wilkins, Baltimore, 1958.
5. Freund, K. and Srnec, J. Zum Problem der allgemeinen Merkschwäche. Ein Modellversuch. Mschr. Psychiat. Neurol., **131:** 226–246, 1956.
6. Gregor, A. and Römer, H. Beiträge zur Kenntnis der Gedächtnisstörung bei der Korsakowschen Psychose, Mschr. Psychiat. Neurol., **21:** 19–46 & 144–167, 1907.
7. Grünthal, E. Zur Kenntnis der Psychopathologie des Korsakowschen Symptomenkomplexes, Mschr. Psychiat. Neurol., **53:** 89–132, 1923.
8. Hebb, D. O. The effect of early and late brain injury upon test scores, and the nature of normal adult intelligence, Proc. Am. Philosoph. Soc., **85:** 275–292, 1942.
9. Korsakoff, S. Über eine besondere Form psychischer Störung, Arch. Psychiat., **21:** 669–704, 1890.
10. Müller-Suur, H. Beitrag zur Frage des Korsakow-Syndroms und der Analyse der amnestisch-strukturellen Demenz, Arch. Psychiat., **181:** 683–711, 1949.
11. Ovsiankina, M. Die Wiederaufnahme unterbrochener Handlungen, Psychol. Forsch., **11:** 302–379, 1928.
12. Pick, A. Beiträge zur Pathologie des Denkverlaufes beim Korsakoff, Ztschr. Neurol. u. Psychiat., **28:** 344–383, 1915.
13. Russell, W. R. *Brain—Memory—Learning.* Oxford Univ. Press, Oxford, 1959.
14. Scheid, W. Zur Pathopsychologie des Korsakow-Syndroms Ztschr. Neurol. u. Psychiat., **151:** 346–369, 1934.
15. Talland, G. A. The interference theory of forgetting and the amnesic syndrome, J. Abnorm. & Social Psychol., **59:** 10–16, 1959.
16. Talland, T. A. Psychological studies of Korsakoff's psychosis: II. Perceptual functions, J. Nerv. & Ment. Dis., **127:** 197–219, 1958.
17. Talland, G. A. Psychological studies of Korsakoff's psychosis: III. Concept formation, J. Nerv. & Ment. Dis., **128:** 214–226, 1959.
18. Talland, G. A. and Miller, A. Perceptual sets in Korsakoff's psychosis. J. Abnorm. & Social Psychol., **58:** 234–240, 1959.
19. Victor, M., Talland, G. A. and Adams, R. D. Psychological studies of Korsakoff's psychosis: I. General intellectual functions. J. Nerv. & Ment. Dis., **128:** 528–537, 1959.
20. Wilcoxon, F. *Some Rapid Approximate Statistical Procedures.* Am. Cyanamid Co., New York, 1949.

EFFECTS OF MOTIVATING INSTRUCTIONS ON REACTION TIME IN SCHIZOPHRENIA[1]

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Both schizophrenic and brain-damaged patients show retardation in simple and choice reaction time (2, 4, 5, 6). Current conceptualizations of the basic pathology involved tend to assume that the essential determinants are rather different in the two conditions. Motivational factors of either a biological or social nature are likely to be implicated to account for the retardation in reaction time of the schizophrenics, while structural factors, reflected in impaired cerebral efficiency, are typically held responsible for the retardation in patients with brain damage. If this is so, it is reasonable to suppose that manipulation of motivational variables of either a biological or interpersonal nature should affect the performances of schizophrenics more markedly than those of patients with cerebral disease. That such manipulation can influence the reaction times of schizophrenic patients has been shown by Rosenbaum, Mackavey and Grisell (7), who found an accelerative effect of shock on simple reaction time in these patients. However, two recent studies have demonstrated similar effects of motivational variables in brain-damaged patients. Blackburn (3) found that a special "urging" condition resulted in a significant acceleration of choice reaction time in these patients and Shankweiler (8) has reported the same effect for failure instructions. In neither study were the gains in speed on retest found to be significantly related to initial reaction time.

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The relative effectiveness of various types of motivational manipulation in the two diagnostic categories can be assessed only on the basis of quite comparable studies. The investigation to be reported presents such a comparison. Utilizing the same procedure which had been employed by Blackburn (3) with brain-damaged patients, the effects of his special "urging" or "evaluative" instructional condition on choice reaction time in schizophrenic patients were determined and compared with his own findings.

METHOD

Sixty male schizophrenic patients and 60 male control patients were given two consecutive administrations of a choice visual reaction time task. The first administration was always given under standard instructions to react as quickly as possible. The second administration was given either under standard instructions or under the special urging and evaluating instructional condition described by Blackburn, one half of the patients in each diagnostic category being assigned to each instructional subgroup. These standard and "urging" instructions were as follows:

Standard or task-orienting instructions: "Now, let's try this choice test again. The same instructions apply as before. Let's have a few warm-ups first."

Urging and evaluating instructions: "Now let's try this choice test again. The same instructions apply as before, only this time, I want to see just how *very* fast you can make the reactions. I've just figured your scores for the last series and your average time was ..... You should be able to do better than that. This time

after each reaction, I will tell you in hundredths of a second how long it took you to react. Try to adjust your reactions so as to continually do better. Knowing how you are doing each time should help you. Let's have a few warm-ups first." (After each trial, the experimenter accurately reports the time and makes evaluative comments. Times equal to the average ± .03 second elicit 'OK'; slower times elicit 'poor' or 'too slow'; faster times elicit 'good' or "fine." In each case, the patient is urged to do even better.)

The apparatus and general procedure were identical with those employed in previous studies (1, 2, 3, 4, 8). The criterion measure on which the analyses were based was the "gain score" utilized by Blackburn, *viz.*, the difference between initial reaction time under standard instructions and retest reaction time under either standard or special motivating instructions.

The control subjects were medical patients who showed no evidence or history of psychosis, cerebral disease, mental deficiency or hospitalization for a psychiatric disorder. Mean age of the 30 schizophrenic patients who received two administrations under standard instructions was 33 years and mean eductional level was nine years. Mean age of the 30 schizophrenic patients who received the special motivating instructions on retest was 34 years and mean educational level was ten years. Mean age of the 30 control patients who received two administrations under standard instructions was 36 years and mean educational level was ten years. Mean age of the 30 control patients who received the special motivating instructions on retest was 37 years and mean educational level was nine years. As estimated by t-tests, there were no significant differences among the subgroups with respect to mean age or educational level.

RESULTS

Analysis of Gain Scores. The mean gain scores of the two diagnostic groups under the two retest conditions are shown in Table 1. It will be seen that retest under standard instructions resulted in a very slight acceleration in reaction time in both groups while retest under the special urging and relaxing instructional condition resulted in a more impressive acceleration. These findings were evaluated by a 2 × 2 analysis of variance which showed a significant main effect for treatments ($F = 34.72$, df = 1, 116; $p < .001$), indicating greater improvement under urging retest instructions than under standard retest instructions. The effect of diagnostic category was nonsignificant ($F = 2.71$, df = 1, 116; $.20 > .10$). The interaction between treatments and diagnostic category was also nonsignificant ($F < 1.0$), *i.e.*, the schizophrenics and controls did not respond differentially to the two types of retest instructions.

TABLE 1

Gain Scores in .001 Sec. of Schizophrenic and Control Patients under Two Types of Retest Instructions

Population	Standard		Urge	
	M	*SD*	*M*	*SD*
Schizophrenic	6	29	40	30
Control	2	25	28	27

As would be expected, the mean initial reaction time of the schizophrenic patients (350 msec.) was significantly slower than that of the control patients (298 msec.) In consonance with previous findings, no significant relationships between gain scores and initial reaction times were found ($r = .24$ for the subjects retested under standard instructions; $r = .16$ for the subjects retested under urging instructions).

Comparison with Brain-Damaged Patients. The brain-damaged patients in Blackburn's study made a mean gain of 42 msec. under the special urging instructions, as compared with the mean gain of 40 msec. made by our schizophrenic patients. However, Blackburn's brain-damaged patients showed a retardation in reaction time (13

msec.) on retest under standard instructions while our schizophrenic patients showed a slight acceleration (6 msec.). This difference in the mean "gain" scores of the two diagnostic groups under standard instructions was found to be significant, as estimated by the t-test ($t = 2.88$; $p < .01$).

DISCUSSION

The results show that the response of schizophrenic patients to special motivating instructions designed to accelerate reaction time is neither greater nor less than that manifested by either brain-damaged or control patients. All three types of patient accelerate significantly to such instructions. These findings indicate that the observation that schizophrenic patients show slower and more variable reaction times than normal subjects under standard instructional conditions and may improve under special motivational instructions cannot be taken to mean that they are suffering from a distinctive motivational deficit.

Essentially the same findings with respect to mean reaction time were secured by Rosenbaum *et al.* (7) in their study of the effects of shock motivation in schizophrenics and normal subjects. Both groups showed a significant acceleration, the interaction between the shock effect and diagnostic category being nonsignificant. They did find that variability in reaction time was decreased to a significantly greater extent in the schizophrenics than in the normal subjects as a function of the shock stimulation. However, the latter finding requires further analysis before its significance is clear. Specifically, the relations between initial variability and change in variability as a function of the shock needs to be determined to insure that the observed difference in decreased variability in the two diagnostic groups is not a function of differences in initial score.

The schizophrenic and brain-damaged patients appeared to show different trends in performance under standard retest instructions. The brain-damaged patients showed an apparent negative practice effect of slight magnitude while the schizophrenic patients showed the apparent positive practice effect of slight magnitude characteristic of control patients (1, 3). If a motivational explanation is applied to this finding, it is obvious that it is the brain-damaged patient who must be assigned the "motivational deficit."

The general implication of these findings is that there is need for caution in interpreting change in responsiveness on the part of schizophrenic patients to motivational manipulation as evidence for a distinctive motivational deficit in these patients. Such an interpretation is tenable only when it has been demonstrated that the observed changes are not characteristic of other types of subject and are not a function of level of initial performance independently of diagnostic category.

SUMMARY

The purpose of this study was to determine the effects of special motivating instructions on choice reaction time in schizophrenic patients and to compare the findings with those previously secured by Blackburn (3) under the same conditions on brain-damaged patients. The special motivating instructions resulted in an acceleration in reaction time in the schizophrenic patients which was almost identical in size with that previously observed in brain-damaged patients. Under standard instructions, both schizophrenic and control patients showed an apparent positive practice effect of slight magnitude. In both instances, this effect was found to differ significantly from the apparent negative practice effect of slight magnitude shown by brain-damaged patients.

The findings indicate that there is need for caution in interpreting change in responsiveness on the part of schizophrenic patients to motivational manipulation as evidence for a distinctive motivational defi-

cit in these patients. Such an interpretation is tenable only when it has been demonstrated that the observed change is not characteristic of other types of subject and is not a function of level of performance under standard conditions independently of the factor of diagnostic category.

REFERENCES

1. Benton, A. L. and Blackburn, H. L. Practice effects in reaction time tasks in brain-injured subjects. J. Abnorm. & Social Psychol., **54:** 109–113, 1957.
2. Benton, A. L., Jentsch, R. C. and Wahler, H. J. Simple and choice reaction times in schizophrenia. A.M.A. Arch. Neurol. & Psychiat., **81:** 373–376, 1959.
3. Blackburn, H. L. Effects of motivating instructions on reaction time in cerebral disease. J. Abnorm. & Social Psychol., **56:** 359–366, 1958.
4. Blackburn, H. L. and Benton, A. L. Simple and choice reaction time in cerebral disease. Conf. neurol., **15:** 327–338, 1955.
5. Huston, P. E., Shakow, D. and Riggs, L. A. Studies of motor function in schizophrenia: Reaction time. J. Gen. Psychol., **16:** 39–82, 1937.
6. King, H. E. *Psychomotor Aspects of Mental Disease*. Harvard Univ. Press, Cambridge, 1954.
7. Rosenbaum, G., Mackavey, W. R. and Grisell, J. L. Effects of biological and social motivation on schizophrenic reaction time. J. Abnorm. & Social Psychol., **54:** 364–368, 1957.
8. Shankweiler, D. P. Effects of success and failure instructions on reaction time in brain-injured patients. J. Comp. & Physiol. Psychol. In press.

LYSERGIC ACID DIETHYLAMIDE: SIDE EFFECTS AND COMPLICATIONS

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Psychotomimetic agents are coming into more widespread use both as investigative tools and as an aid in psychotherapy. The rationale for the induction of reversible psychotic-like phenomena cannot be considered in detail here. It can be mentioned, however, that such techniques offer a further understanding of the determinants of the naturally occurring psychoses. With these chemical devices, study of isolated elements of normal and abnormal mental function, for example, perception or hallucinations, becomes a laboratory possibility. The state may be employed to screen drugs for clinical use. A subjective appreciation of psychotic symptomatology for personnel in contact with disturbed patients is now available. An important feature of the psychotherapeutic application is that, without impairing mental clarity, defensiveness is reduced and significant unconscious material might be uncovered. Lysergic acid diethylamide (LSD) and mescaline are currently the most dependable drugs capable of producing transient dissociation states for these purposes.

Reports of untoward events occurring in connection with the experimental or therapeutic use of the hallucinogens have been surprisingly infrequent. Agents which call forth such profound alterations of ego structure, awareness, cognition and affect might be occasionally expected to induce adverse reactions.

In order to ascertain whether such incidents were occurring but not being reported, a questionnaire was sent to 62 investigators who had experience with either LSD or mescaline in normal subjects or patients. Most of these physicians had published on their work with the hallucinogens. Others were referred to us as actively involved in the study of these agents either as a therapeutic adjunct or as a research instrument in human investigations. They were asked for the following information:

1. The number of individuals who had received either LSD or mescaline.
2. The average number of times these drugs were given to each person.
3. The number of major complications encountered. Specific inquiry about suicides, suicide attempts, prolonged psychotic reactions and prolonged depressive reactions was made. When mention of such a complication occurred a summary of the case was requested.
4. The precautions taken by the respondent prior to administration of these drugs.
5. The diagnostic groups excluded from LSD or mescaline administration.

Replies from 44 of the 62 inquiries were received. It cannot be assumed that the responses are necessarily representative, but it should be noted that this yield represents data on almost five thousand individuals who had received either LSD or mescaline on more than 25,000 occasions. The number of times these agents were administered to a single person varied from one to 80. Dosages for LSD ranged from 25–1500 mcg., mescaline was given in 200–1200 mg. amounts. Although this report will deal with LSD, information concerning mescaline is included because the psychic activity of both agents is considered similar.

Adverse responses tended to occur at the higher dosage levels (above 75 mcg. LSD or 400 mg. mescaline) but this was by no means invariable. No instance of serious, prolonged physical side effects was found either in the literature or in the answers to the question-

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naire. When major untoward reactions occurred they were almost always due to psychological factors.

REVIEW OF LITERATURE

Elkes, Elkes and Mayer-Gross (6) have expressed their concern that an occasional experimental subject may be a danger to himself and others. Even normal volunteers might have delayed or severe responses to LSD lasting several days. An early psychotic condition could be aggravated by exposure to such an experience. For these reasons these investigators recommend that the hallucinogenic drugs be used in hospital situations where constant supervision by trained personnel is available.

Savage (9) has noted the completed suicide of a depressed, chronically schizophrenic girl who had been given LSD. Her defensive pattern changed from one of nihilistic delusions of being dead and having no body to that of rage and resentment against parents and therapist. A few weeks later she was allowed to go home for a visit and used this opportunity to throw herself under a train. He also records a depressive reaction lasting for a day which occurred after the ingestion of 150 gamma of LSD. The patient had taken the drug without the therapist's knowledge, but called him after four hours. She later said "I would have died if you hadn't been there." In another instance where the drug (100 mcg.) was taken alone the subject became overwhelmed with intense fears, delusional ideas and complete loss of contact. Recovery was gradual over the next week.

Savage found that conversation or performance tests act to diminish the intensity of the reaction whereas anxiety, isolation or stress increases it. The dosage factor appears important with the larger doses permitting a greater likelihood of becoming overwhelmed by paranoid thinking, suspicion and acting out. Self-experiments without invigilators or neglect of the subject can be dangerous.

In a patient with a lifelong pattern of day dreaming, Stevenson (10) witnessed a psychotic-like state that lasted for a week. The actual experience had been a profound one with considerable depersonalization. Three days later delusional thinking and considerable hypochondriasis was observed. The patient was seen in therapeutic interviews and made a complete recovery.

Three interesting delayed reactions to mescaline are related by Harley-Mason, *et al.* (7). In each instance these were associated with either excessive fatigue or stress. For example, one patient two weeks after exposure to 400 mg. of mescaline became physically and mentally exhausted. She saw dark, moving objects, and with her eyes closed, dull colored, hypnagogic imagery.

Cooper (3) has also noted the recrudescence of LSD-like effects weeks or months afterwards. This consists of brief episodes of inappropriate mood swings, spatial and temporal distortions, changes in body image and occasional auditory and visual illusions or hallucinations.

The potential dangers in the use of LSD were reviewed by Eisner and Cohen (5). The possibilities of treatment precipitated depression, suicide and psychosis were discussed. Some speculations about the post-LSD reappearance of transient dissociative phenomena in an occasional patient was offered. It was suggested that if this drug did make unconscious fantasy material more available, it might also lower the threshhold for subsequent similar experiences. Favorable conditions for the spontaneous re-emergence of primary process elements seem to be extreme tension, meditation and states of relative restriction of sensory inflow. The patient should be made aware of this remote contingency for it is the inability to account for the event that makes it frightening and potentially hazardous.

In summary, the literature directly records only one suicide and that in a schizophrenic patient, and a small number of short,

self-limited psychotic reactions and other lesser side effects. Turning to the questionnaire additional information of assistance to the investigator using LSD becomes available.

IMMEDIATE ADVERSE REACTIONS

Although data on untoward events during the LSD state was not requested, a number of fleeting but impressive incidents were related in response to our inquiry. Osmond[2] has seen an epinephrine-like reaction with anxiety, pallor, a cold sweat, thready pulse and dilated pupils. The only convulsion noted was described by Sandison. The incidence of seizures is so low that one wonders whether coincidence might explain the single convulsion reported. The most common, but still infrequent, immediate problem was one of unmanageability. This apparently occurs when insight into the situation is lost and the individual acts upon delusory, usually paranoidal, ideas. Instances of running away from the tester, disrobing, or accidental self injury were described. For example, a medical student given 125 mcg. developed an acute, hyperactive paranoid state which required restraints for three hours.

Panic episodes were likewise mentioned. When these develop early they seem to represent the terror involved with the loss of ego controls. At the height of the reaction panic may be precipitated by the mobilization of aggressive impulses or by the upsurge of considerable guilt-laden material. Finally, after many hours of frightening dissociation the subject could develop an intense fear that he will not be able to get back to his ordinary state.

Severe physical complaints can dominate the entire experience. Those subjects whose major defensive response is somatization have been able to fight off the psychic effects of the drug at the cost of suffering a variety of aches and pains for six hours. Osmond warns of the occasional appearance of a severe catatonic state. We have reported one which was impressive to observe (2).

In this regard it may be well to consider which groups are more likely to have unpleasant, painful reactions to LSD. Those with excessive initial apprehension, rigid but brittle defensive structures, or considerable subsurface guilt and conflict could have difficulties. Although there are exceptions, people who find that the implications posed by the LSD experience are contrary to their basic philosophies become dysphoric. Invariably, those who take hallucinogenic agents to demonstrate that they have no value in psychiatric exploration have an unhappy time of it. In a small series of four psychoanalysts who took 100 gamma of LSD, all had dysphoric responses. Two Zen Buddists were given LSD in order to compare the drug state with the transcendent state achieved through meditation. Both Zen teachers became so uncomfortable that termination with chlorpromazine became necessary.

In the immediate post-LSD period certain undesirable occurrences have been mentioned and it is well to be aware of these possibilities. The first is a simple prolongation of the LSD state. Ordinarily, after a night's rest it is to be expected that complete cessation of the drug effect will have occurred. However, the persistence of anxiety or the visual aberrations for another day or two in wavelike undulations has been described. Isbell reports five such instances in drug addicts given 1–3 mcg/kilo. Feld speaks of a psychology trainee who took the drug for experiential purposes and had to be given phenothiazines and kept on a locked ward for a day because of excitement. An almost identical case was seen by Mayer-Gross. A psychology student was given 120 mcg. as part of an experiment in the biochemistry laboratory. She remained in a state of agitation and motor restlessness for two days. She recovered and has remained well during a seven-year followup.

A valuable point is illustrated by Merlis'

[2] Where bibliographic reference numbers are not used, the quoted material derives from the questionnaire.

three patients who were left alone after the interview period was completed. The drug effects were declining and it was assumed that they were recovering uneventfully. Instead, they became increasingly tense and confused and required further therapeutic support. This exemplifies the importance of constant attendance even during the waning phase of the psychotomimetic experience.

More frequently remarked upon were short-lived depressions. These have been seen by a number of the correspondents as well as by the writer. A variety of possible causative factors are evident. The depression may simply be the letdown after the drug induced hyperphoria and feeling of self transcendence. If the experience was characterized by an emergence of considerable shame or guilt, an inability to integrate or re-repress the released memories may induce a brief depressive reaction. In the therapeutic situation when the insights acquired during the drug sessions are not translated into altered patterns of behavior and of dealing with people then aggressions may be turned inward (5).

SUICIDE

An analysis of the data on successful and unsuccessful suicide attempts reveals that in only a very few instances a direct connection between the LSD experience and the movement toward self-destruction could be discerned. Some of the reports stated that the suicidal incident was mentioned for completeness rather than because of a conviction that a causal relationship existed. On the other hand, genuine efforts to end one's life have apparently also been seen.

SUICIDE ATTEMPTS

Drowning is considered to be preferred by suicidal LSD patients according to Sandison. Two of his patients attempted to drown themselves and other patients reported drowning fantasies. Although drowning as a preferential mode of destruction is not noted by others, it is interesting to speculate that death in the grand manner could be considered by those who have achieved a state of complete ego dissolution.

Gilberti treated an obsessive compulsive with a depersonalization syndrome with average amounts of LSD combined with psychotherapy. There was no improvement. A month or two later the patient attempted suicide, was hospitalized and improved after insulin coma therapy.

Ling's case is an example of a devastating insight which overwhelmed the defensive position. Under the drug the patient vividly relieved a period at age two when his father had been in the Navy and his mother had given her "love" indiscriminately and promiscuously to all men except the patient. This uncovered information in a markedly disturbed person produced a depression and attempt at suicide. With intensive psychotherapy he recovered from the depression.

A psychiatric resident in our hospital wanted to see what LSD would do for one of his patients that had not been moving in psychotherapy. The diagnosis was chronic anxiety in a schizoid personality. Twenty-five micrograms were given; during the next few hours the patient kept repeating "I see it all now," but refused to communicate with the therapist. Three days later he scratched his wrists with a razor blade. The depression lifted slowly and he was eventually discharged from the hospital essentially unimproved.

COMPLETED SUICIDES

Consummated suicides attributable to LSD are indeed rare. Savage's case (1) has been referred to already. Stoll, during a visit to this country, spoke of a woman who had been given the drug without her knowledge. The devastating effects of a completely unexplicable psychic disruption were seemingly too much for this person to endure and she took her life.

In response to our questionnaire Hoff related that after two 30 mcg. sessions a patient became depressed for three weeks and

then committed suicide. No further details were given.

A physician who had habitually inhaled nitrous oxide for many years was given 150 mcg. of LSD. Six months afterwards he was found dead in his room with the NO_2 mask on his face. The respondent (Janiger) does not consider that this suicide was the result of LSD administration, rather the occurrence was mentioned "for the record." From the circumstances it may be questioned that suicide had even been contemplated.

A 44 year old suicidally depressed female who was addicted to Demerol was given 50 mcg. of LSD by Hartman. Three previous suicidal attempts had been made and 50 electroshock treatments had been administered in the past. Hospitalization was refused by the patient because of her fear of further shock treatments. The LSD session was marked by the ventilation of some hostility. Five days later she became involved in an argument with her husband who then left her alone against the orders of her physician. She swallowed a lethal amount of snail poison.

It is noteworthy that all the suicidal acts have been in disturbed patients rather than normal subjects. In addition, their response to psychotherapy with LSD had been poor. From the information available these were a seriously disturbed group prior to treatment with LSD. The establishment of improved criteria for the selection of patients and increased attention to the patient who is not progressing under LSD therapy can reduce even further the remote possibility of suicide. There are no reports that LSD itself has been used as a method for committing suicide.

PROLONGED PSYCHOTIC REACTIONS

A number of psychotic breakdowns in association with LSD were reported to us. Hoch and Malitz relate the interesting story of two 30 year old identical twins who were given 180 mcg. of LSD intravenously. One was schizophrenic; he became more autistic, affectively disordered and in poorer contact. The other twin was brought in as a "normal" control. He reacted with somatic and perceptual disturbances but had recovered by evening and left the hospital. Two days later he developed nausea, tension, a feeling of immobilization, anxiety, depersonalization and preoccupation with a "dream" he had under LSD. He was admitted to the hospital where mild barbiturate sedation was given. Five days later he was discharged and returned to work.

A 25 year old preschizophrenic latent homosexual with many neurotic fixations was mentioned by van Rhijn. He received 200 gamma of LSD with the result that the schizophrenic features became more obvious. His behavior became bizarre and he required hospitalization. The final outcome was not reported.

Hoff reports one and Sandison two cases of prolonged psychotic reactions in patients with dosages in the 100–200 mcg. range. Recovery was incomplete in one of these patients.

Cameron tells of a 23 year old withdrawn, depressed male patient who had had hallucinatory experiences in the past. After the administration of 100 mcg. and the completion of the therapeutic interview he barricaded himself into a room and made an abortive suicidal attempt. The psychotic manifestations persisted for a fortnight and was terminated with 48 hours of deep sleep therapy.

A patient of Janiger's had taken peyote clandestinely before and shortly after two treatments with 125 and 150 mcg. of LSD. He went into what might be described as a chronic LSD state for weeks, culminating in an undifferentiated schizophrenic reaction for which he was hospitalized and treated with phenothiazines. Over a period of six months he made a slow but complete recovery.

A patient at the Metropolitan State Hospital[3] was recently brought to our attention.

[3] Permission to examine the case record and

He is a 31 year old, divorced male. Since 1951 when he had been a participant observer at the atomic explosion at Eniwietok, he had noted increasing anxiety. It was during this voyage that he received a "Dear John" letter from his wife. Subsequently, the blast was interpreted by him as a manifestation of God's power, at other times it was the serpent in the Garden of Eden.

He developed an intolerance to noise, shakiness especially when around people, fears of heights and elevators, and a phobia about getting his hair cut. There was preoccupation with the significance of his bowel movements. Help was sought from various religious groups and finally he entered the Catholic church. His priest recommended psychiatric care and for two years a therapist saw him two or three times weekly. Apparently he was exposed to an unusual variety of treatments including dream analysis, spiritual readings, reincarnation discussions, a novel sort of group therapy and hypnosis. When no particular response to these procedures took place the therapist gave him LSD in 75, 125 and 175 mcg. doses at weekly intervals. The technique used was rather unconventional. The patient was blindfolded; occasionally the therapist would come into the room and ask him to describe his sensations. After the first session he was depressed for two or three days. The second treatment was the most significant. During it, he clearly saw in great detail, how as a child of four he had smothered his baby brother in order to keep him from crying. He had no previous conscious awareness of the "murder," but has always had a feeling that something bad had happened when he was very young. This material was tape-recorded, as the therapist was not present during parts of this session.

After termination of the interview the memory was so strong and convincing that he went to the police and "confessed." Whether this incident was fact or fancy could not be established. He was not detained by the police. However, there was an upsurge of agitation, confusion and depression which was not changed by the final LSD interview.

Shortly thereafter, he voluntarily committed himself to Metropolitan State Hospital. At the time of admission poor insight, ideas of reference, flattened affect, circumstantiality and moderate anxiety were described. Psychological testing indicated that the patient was a decompensating schizophrenic who was desperately struggling to reestablish his shattered defenses. He improved slowly over the next half-year without specific therapy.

This case is described in some detail because it illustrates a number of correctible deficiencies which entered into the patient's management.

1. The therapist was possibly a rather disturbed person himself who favored unconventional methods of treatment. His personal experience with LSD as a therapeutic agent was limited.

2. The therapist did not deal with the highly traumatic material as it arose, resolving the guilt feelings, giving support, etc. Instead of a disaster, the second session may well have been highly therapeutic.

3. The patient was blindfolded and left alone for long periods. This in itself might well evoke panic. There should have been constant contact with the therapist or other trained person.

4. It may be that LSD was relatively contraindicated for the patient. Incipient schizophrenics are considered increased risks for this type of therapy.

Of the eight instances of psychotic reactions lasting more than 48 hours that were reported in response to our questionnaire, only one was in an experimental subject and that subsided within a few days. It is to be recalled that he was the identical twin of a schizophrenic. The remaining seven cases occurred in patients undergoing therapy. Two of these went into a remission within a

interview the patient was granted by Dr. Robert Wyers, Superintendent, Metropolitan State Hospital, Norwalk, California..

TABLE 1
Estimated Rates of Major Complications Associated with LSD

	Attempted Suicide	Completed Suicide	Psychotic reaction over 48 hours
Experimental subjects	0/1000	0/1000	0.8/1000
Patients undergoing therapy	1.2/1000	0.4/1000	1.8/1000

few weeks and the other five had either prolonged courses or the details were insufficient to establish the outcome.

A tabulation of the material supplied in the survey indicates the approximate incidence of the important complications encountered (Table 1).

ADDICTION

No instance of addiction to LSD was reported. Physiological addiction is unlikely because of the extremely rapid onset of tolerance (1). Psychological habituation is conceivable but the groups prone to addiction, the immature dependent or the acting out psychopath, are more likely to have an unpleasant than an euphoric response to LSD. None of the respondents indicate that the individuals who achieve a mystical state with the assistance of this drug have become habituated. As an investigative drug the controlled supply of LSD does not permit a final answer to the question of addiction. If it should become generally available we will obtain confirmation or denial of our opinions concerning its nonaddictability.

PRECAUTIONS

SCREENING

Many investigators insist upon a preliminary physical and psychiatric examination of subjects. A family or personal history of nervous breakdown is sufficient to exclude volunteers from some studies. Occasionally, a liver panel, electrocardiogram, MMPI or other psychologic screening test is required. Most commonly, a psychiatric interview with the prospective candidate is considered sufficient for selection of experimental subjects. The interview is also used for orientation, to establish rapport and to answer questions which may be bothering the volunteer. In some institutions signed releases are obtained.

The patient considered for LSD is probably fairly well known to the therapist. His selection is an individualized problem, and certain relative contraindications will be discussed later. His briefing is a matter of some importance, with the value of the drug interview sometimes depending on the preliminary instructions. Something of the nature of the experience and the expectations for the session are communicated at this time. Misconceptions are corrected and necessary reassurrances are given.

DURING THE SESSION

That the person under the influence of LSD should not be left alone is universally agreed. Human contact is comforting and serves as a pivot between every day reality and the strange world of LSD. Without it the patient can readily lose all orientation. Personnel in contact with the subject should be experienced and sympathetic. Control of the subject through continuous observation by trained and understanding workers is one of the more important preventative measures that can be taken.

The significance of personnel attitudes and of the setting for the therapeutic application of LSD should be mentioned. The state is a highly suggestive one with the patient responding strongly to environmental cues. He can sense the therapist's unspoken feelings with phenomenal accuracy. Impersonality, coldness and disinterest is the equivalent of being left alone.

Although rarely needed, LSD antagonists should be available. Chlorpromazine is the most satisfactory agent for termination. When a rapid effect is desired 25–50 mg parenterally is given, 50 mg orally acts slower but is effective in a half hour. These

amounts can be repeated if necessary. The other phenothiazines have not been used as frequently and those with a piperazine ring in the side chain may not equal chlorpromazine in reversing the LSD state. The action of azacyclonal is dubious. Reserpine has occasionally intensified the reaction. Nicotinic acid is successfully used by one group. Intravenous or intramuscular sodium amytal in 0.375–0.75 Gm. amounts is an effective agent in aborting LSD activity.

POST-LSD CONSIDERATIONS

Normal volunteers are ordinarily allowed to leave the hospital eight hours after an average dose has been ingested. However, they are not permitted to drive and they should spend the evening quietly at home with someone who knows the approximate nature of their experience. The opportunity for telephonic contact with the investigator ought to be possible. Sometimes a sedative is routinely prescribed at bedtime.

The outpatient receiving LSD is required to stay in the hospital overnight by many therapists. He remains in a room with a nurse or attendant in the adjacent area. Sleeping medicine is available if needed. Nondrug interviews shortly afterwards are recommended to re-order and re-evaluate the emotional and intellectual elements of the LSD experience. Sandison suggests more followup care be given those who have had 150 mcg. or more.

CONTRAINDICATIONS

Naturally, detectable neuropsychiatric disease in volunteers and paid subjects is cause for exclusion from experimental work requiring a relatively normal group. It is surprising how often serious psychopathology is found among these people. It is entirely possible that LSD and mescaline attract certain unstable individuals in their search for some magical intervention.

With respect to patient selection, there is general agreement that markedly schizoid personalities or compensated schizophrenics should be excluded because of the possibility of precipitation into a psychosis. The established schizophrenic also tends to do poorly with the hallucinogens, yet a variable degree of success in their treatment has been reported using special techniques. No one is inclined to consider the organic psychotic as a candidate for LSD therapy. The epileptic is also ordinarily excluded although prudence rather than evidence dictates this restriction. The mentally retarded patient would seem to be a poor choice.

Serious, active physical disease is a contraindication to therapy if only because the stress of an LSD experience can be exhausting. Nevertheless, following Huxley's and Heard's (8) suggestion, we have given LSD to a small number of terminal cancer patients, who had difficulty accepting the idea of their personal death, without untoward effects.

Since these drugs are detoxified in the liver (11), damage of that organ is assumed to be a bar to treatment. This restriction may be more rational with regard to mescaline than LSD because the latter drug was administered to a series of unselected Skid Row alcoholics (4) many of whom had fatty livers or cirrhosis, without unusual sequellae.

Individual therapists would avoid placing obsessive compulsives, hysterical or acutely anxious and agitated patients into the treatment situation. Others feel that these groups are the ones that respond best to LSD therapy. The seriously depressed patient is avoided by some because of the danger of suicide. Although the risk is greater, we are inclined to think that suicide can also be averted with LSD in selected depressed patients. However, they must be kept in a completely controlled situation. The precise contraindications have not yet been worked out for the neurotic patient.

The paranoid personality should be regarded dubiously with respect to LSD. On occasion, one of them will become grandiose as a result of a mystical experience under the drug and will use this as final proof of a

hitherto only suspected omnipotence. In one case that was indirectly observed (5) systematized delusions concerning LSD and religion developed. This happened to be the therapist's first case in which LSD was used and he reacted to the heady and extremely well-structured delusory schemes by going along with them initially. This points up the requirement that the doctor who employs LSD as a psychotherapeutic adjunct be a mature person. It is conceivable that LSD may serve as a gratification for the therapist's own needs for power.

MESCALINE

Although this survey dealt primarily with lysergic acid diethylamide, information with regard to side effects with mescaline was also received. In general these tended to duplicate comments submitted with reference to the former drug.

The well known proclivity for mescaline to produce some nausea and, less frequently, emesis was again noted. Two of Denber's patients sustained a shock-like state ten minutes after receiving 500 mg. intravenously. The blood pressure fell, the pulse became imperceptible, and the skin was ashen and cold. Anxiety and agitation were obvious. Intravenous sodium amytal blocked these effects in one case and chlorpromazine in the other. Denber suspects that a paroxysmal cardiac irregularity may have been causative. A severe panic reaction was witnessed by Smythies requiring termination of the experiment with intravenous sodium amytal.

The fleeting recurrence of the mescaline state after a period of complete recovery was listed by four investigators. One wonders whether this phasic relapse may not be somewhat more frequent with mescaline than with LSD.

Stevenson gave 400 mg. of mescaline to a young girl who proceeded to have auditory hallucinations and doubts about the reality of perceived objects for several days thereafter. She made an uneventful recovery without residuals except for a distaste for mescaline.

DISCUSSION

This report of adverse effects and complications to the more common psychotomimetic drugs is doubtless incomplete. However, it must be generally representative of the gamut of mishaps that might be encountered. By far, the greatest morbidity and mortality occurs in patients rather than experimental subjects. How it compares in this regard to other treatment modalities is quite unknown. A search of the literature for a statistical report on the incidence of suicide during psychoanalysis or other forms of psychotherapy was fruitless.

The hallucinogenic experience is so striking that many subsequent disturbances may be attributed to it without further justification. The highly suggestible or hysterical individual would tend to focus on his LSD experience to explain subsequent illness. Patients have complained to Abramson that their LSD exposure produced migraine headaches and attacks of influenza up to a year later. One Chinese girl became paraplegic and ascribed this catastrophe to LSD. It so happened that these people were all in the control group and had received nothing but tap water.

Abramson reports no complications in his large series and is inclined to think that a placebo effect accounts for many of the mishaps observed by others. That this is plausible is demonstrated by Busch's comment that the only suicide attempt he has seen was in his control group. An immediate, severe skin reaction following the ingestion of distilled water as an LSD placebo is mentioned by Ditman.

The physician might likewise be inclined to attribute undesirable incidents that arise to an unique and potent psychochemical. This could lead to an overreporting of side effects. Conversely, serious complications

may sometimes go unreported because the investigator has guilt feelings about the matter.

The precautions which could reduce the incidence of untoward incidents may be briefly summarized.

1. The careful and thoughtful selection of subjects and patients is a necessity. For the psychotherapist not too familiar with this modality, particular care in the choice of patients is desirable. Prepsychotic individuals and those whose major defense is paranoid projection are apt to be aberrant reactors.

2. A sufficient level of control of the patient during and after the experience is necessary. The need for constant attendance during the session has been mentioned. Those who move to either extreme of the emotional scale and those whose reality contact is impaired should be appropriately accompanied even when going to the toilet. Hospitalization for 24 hours is justified for patients especially when more than one mcg/kilo is used. Experimental subjects whose LSD state has subsided may be taken home on the conditions that a friend or relative be available and that decision-making of a major nature be delayed until the next day.

3. The patient may require reassurance and support during the active phase of the drug's activity. The physician need not be constantly present, a trained and sympathetic nurse or attendant may substitute for him.

4. The technique of using LSD as a psychiatric adjunct is a special skill. The therapist himself should probably have experienced the LSD state. It appears that complications are more likely with a therapist who is relatively unfamiliar with the agent. Supervision of the first few interviews by a physician experienced in LSD therapy might be desirable.

5. The therapist must be prepared to handle a sudden upheaval of repressed and traumatic memories without permitting the patient to be overwhelmed. The preferred technique for doing psychotherapy with LSD is far from settled. The accelerated recall of memories with strong emotional content requires an active, rather than an expectant, participation by the therapist.

6. Personnel in contact with the LSD patient ought to be specifically trained and understanding of the nature of the state.

7. Measures to counteract the effect of the drug should be at hand.

8. In the days following the exposure the physician must be available for consultation should disturbing symptoms develop.

CONCLUSION

From a review of the literature and the communications of 44 physicians who have administered LSD or mescaline, an attempt to categorize and analyze the potential hazards has been made. This inquiry into the adverse effects of the hallucinogenic drugs indicates that with proper precautions they are safe when given to a selected healthy group. Their use in patients has been associated with an occasional complication. An analysis of these incidents suggests that with the application of certain safeguards many of the side effects might have been avoided.

REFERENCES

1. Cholden, L. S., Kurland, A. and Savage, C. Clinical reactions and tolerance to LSD in chronic schizophrenia. J. Nerv. & Ment. Dis., **122:** 211–221, 1955.
2. Cohen, S., Fichman, L. and Eisner, B. G. Subjective reports of lysergic acid diethylamide in a context of psychological test performance. Am. J. Psychiat., **115:** 30–35, 1958.
3. Cooper, H. A. Hallucinogenic drugs. Lancet, **268:** 1078, 1955.
4. Ditman, K. Personal communication.
5. Eisner, B. G. and Cohen, S. Psychotherapy with lysergic acid diethylamide. J. Nerv. & Ment. Dis., **127:** 528–539, 1958.
6. Elkes, C., Elkes, J. and Mayer-Gross, W. Hallucinogenic drugs. Lancet, **268:** 719, 1955.
7. Harley-Mason, J., Laird, A. H. and Smythies, J. R. The metabolism of mescaline in the human. Confinia neurol., **18:** 152–155, 1958.

8. Huxley, A. and Heard, G. Personal communication.
9. Savage, C. The resolution and subsequent remobilization of resistance by LSD in psychotherapy. J. Nerv. & Ment. Dis., **125:** 434–437, 1957.
10. Stevenson, I. Comments on the psychological effects of mescaline and allied drugs. J. Nerv. & Ment., Dis., **125:** 438–441, 1957.
11. Stoll, A., Rothlin, E., Rutschmann, J. and Schalch, W. R. Distribution and fate of C^{14} labeled LSD-25 in the animal body. Experientia, **11:** 396–399, 1955.

THE RELATIONSHIP OF EXPECTATION OF IMPROVEMENT TO ACTUAL IMPROVEMENT OF HOSPITALIZED PSYCHIATRIC PATIENTS

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INTRODUCTION

In recent years efforts have been made to relate the outcome of psychiatric treatment to factors other than traditional prognostic considerations (diagnosis, length of illness, age at onset, etc.) and the specific treatment undertaken. For example, the personality trait of "ethnocentrism" was found to be negatively correlated with improvement of neurotics in psychotherapy (9), whereas in a study of Gliedman *et al.* (5) no association was found between the nature of patients' incentives for seeking psychotherapy and subsequent improvement. In an earlier investigation the present authors found that improvement in a group of hospitalized psychiatric patients was related to several qualitative factors in the patients' perceptions of the psychotherapeutic situation and the psychiatric hospital and to the overall "favorableness" of their conscious attitudes (2).

Of factors considered as potential influences on the outcome of psychiatric treatment, the patient's expectation of improvement is of particular interest. Several investigators (4, 8) have compared the response of patients to psychotherapy to the placebo reaction seen in drug therapy. It could be that the patient's faith or conviction in the efficacy of a particular type of treatment, and attendant high expectation of improvement, might, acting like a placebo, be a significant determinant of the actual outcome of treatment. The factor of expectation of improvement might also underlie the frequently observed enigma that neurotic patients once placed on waiting lists for psychotherapy often improve measurably (1, 3). In the present research an effort was made to explore specifically the relationship of the patient's expectation of improvement to the actual outcome of treatment.

EVALUATIVE PROCEDURES

The factor of expectation of improvement was measured by two procedures of the Psychiatric Attitudes Battery and the degree of actual improvement ascertained by means of the Degree of Improvement Rating Scale.

PSYCHIATRIC ATTITUDES BATTERY

The complete text and scoring instructions of the Psychiatric Attitudes Battery, together with data relating to its reliability, has been published elsewhere (7); accordingly only a brief description of the two tests pertinent to the present research follows. These are the Picture Attitudes Test and the Sentence Completion Attitudes Test.

The Picture Attitudes Test, a projective technique modeled after Murray's Thematic Apperception Test (6), consists of two cards. The first, or "Patient-Doctor" card, pictures two men conversing in a plainly furnished room with an illegible "diploma" on the wall. An alternate card for female patients pictures a man and a woman in the same situation. The second, or "Psychiatric Hospital" card, pictures

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two women in nurse's uniforms and a man and a woman near a nondescript building. All cards are sufficiently ambiguous in content to allow considerable latitude in interpretation. The cards were presented to the patients in the order given above with the usual TAT instructions—to tell a story describing the situation, what brought it about, and how it is resolved.

The therapeutic outcome projected by the patient into the stories elicited by these cards was used as a measure of the patient's own expectation of improvement. A numerical score of one, two, or three was assigned to each story indicating a high, moderate, or low expectation of improvement, respectively, and a total for the two cards obtained.

The Sentence Completion Attitudes Test of the Psychiatric Attitudes Battery was the second measure of expectation of improvement. Six of the 21 incomplete sentences comprising this test specifically lend themselves to interpretation of expectation of improvement. For example, the sentence, "After psychiatric treatment a person . . . might be completed with . . . adjusts much better, . . . still has some time to go, or . . . is often worse," may be considered as corresponding to a high, moderate, and low expectation of improvement. Again by assigning numerical values of one, two and three to these possibilities and summing the six items, an index of the patient's expectation of improvement was obtained. As with the Picture Attitudes Test, the lower the numerical score, the greater the expectation of improvement.

DEGREE OF IMPROVEMENT RATING SCALE

This scale is being published in its entirety elsewhere as part of a related study (2). The scale is so constructed that comparisons are made of the degree of therapeutic change in patients who may differ widely in the degree of psychiatric impairment present initially, as well as in the nature of their illnesses. Judgment of the patient's condition is not made in any absolute sense but rather in terms of the degree and direction of change in his psychiatric status, using his condition during the first week of hospitalization as a baseline. This is accomplished by defining the eight points along the improvement continuum which constitutes the rating scale in terms of the presence or absence of symptomatic change and of more basic changes in psychopathology relative to the patient's initial condition, as evidenced by specific criteria dealing with his interpersonal adjustment and mental status. The eight categories are designated as follows: 1) apparently well; 2 and 3) symptomatic improvement plus varying degrees of favorable change in underlying psychopathology; 4) symptomatic improvement only; 5) essentially unchanged; 6) symptomatically worse; and 7 and 8) symptomatically worse plus varying degrees of unfavorable change in underlying psychopathology.

ADMINISTRATIVE PROCEDURES

As part of the Psychiatric Attitudes Battery, the two tests were administered to 142 patients at the Institute of Living from one to two weeks after admission. The patient population studied was a random sample of admissions to the hospital. Seven of the patients responded to neither of the tests in scorable fashion, leaving 135 in the study. They ranged in age from 16 to 72 with a median age of 34.7 years. Sixty-two per cent were women. Some 39 per cent of the group had received a substantial amount of psychotherapy out of the hospital and 28 per cent had had somatic therapy (EST or insulin) before the present admission. The group varied widely with respect to other background factors (occupation, educational achievement, socio-economic status, etc.) as well as in length and severity of illness. Diagnostically, 17 per cent were neurotic, 57 per cent psychotic and 26 per cent personality disorders. Although all patients had some psychotherapy, for 64 per cent

this was the principal treatment; 30 per cent had EST and six per cent insulin-coma in addition. Many of the patients had psychotropic drugs and all participated in the hospital program of avocational and social rehabilitation to some extent. This heterogeneity of the group investigated was intentional, the object being to ascertain whether specific attitudinal factors, such as expectation of improvement, might be related to improvement despite the variability of the clinical picture and the commonly considered background and experimental factors.

The degree of improvement of each of the 135 patients in the study was ascertained by means of the Degree of Improvement Rating Scale described above. This was completed by each patient's therapist from four to six months after admission to the hospital. The therapists had no knowledge of their patients' scores on the expectation of improvement tests.

RESULTS

Therapists' ratings on the Degree of Improvement Rating Scale ranged from category 1 (four cases) to 7 (one case) with the greatest number of cases (30 per cent) falling in rating 4 (symptomatic improvement only); the other scores were distributed in an approximately normal fashion about this mode.

The distributions of the scores on the expectation of improvement tests are given in Table 1. The means (and medians) obtained on the two tests correspond to a moderately optimistic outlook about the outcome of hospitalization. Scores above these means correspond to less favorable or to poor expectations of improvement.

The patients were classified according to their improvement ratings and simultaneously for their scores on the two expectation measures, each considered separately. Since some of the frequencies were of very low magnitude, the improvement ratings were combined into two categories. Ratings 1–4 correspond to symptomatic improvement or better and, ratings 5–7 correspond to no change or worse. The expectation scores were divided at the median, separating patients into those with more favorable and less favorable expectation of improvement. Even using this breakdown, which tends to maximize the slight degree of association observed, it can be seen from Table 2 that no statistically significant relationship was established between the two variables.

TABLE 1

Distribution of Scores on Tests of Expectation of Improvement

	Range	Mean	Standard Deviation
Picture Attitudes Test Outcome	2–6	3.21	1.03
Sentence Completion Attitudes Test Outcome	6–15	9.15	1.78

TABLE 2

*Distribution of Patients' Expectations of Outcome Classified According to Independent Judgment of Patient Improvement**

Therapists' Ratings	Measure			
	Picture Attitudes Test Outcome		Sentence Completion Attitudes Test Outcome	
	High expectation (Below median)	Low Expectation (Above median)	High Expectation (Below median)	Low expectation (Above median)
Improved (*1–4*)	55	54	54	54
Unimproved (*5–8*)	11	14	12	14
	$\chi^2 = .34$, n.s.		$\chi^2 = .12$, n.s.	

* Of the 135 patients included in the study, one was scorable on the Picture Attitudes Test only (and was rated improved), and one on the Sentence Completion Test only (and was rated unimproved). This accounts for there being 134 subjects in each contingency table but a difference of one in the improvement rate.

CONCLUSIONS

The data reported here do not corroborate the contention implicit in the literature that the patient's expectation of improve-

ment significantly influences the actual outcome of treatment. It may be that means other than those used in this research to measure the variables concerned would demonstrate such a relationship. The answer to this, of course, awaits further research. It should be pointed out, however, that the test procedures used here (the Psychiatric Attitudes Battery and Degree of Improvement Rating Scale) have elicited statistically significant associations between other attitudinal factors and therapeutic outcome in the same patient population (**2**). It could be conjectured also that a relationship between expectation of improvement and actual outcome might be demonstrable in a less heterogeneous patient group (*e.g.* neurotics only or patients without previous treatment) than the randomized population used in this study.

REFERENCES

1. Barron, F. and Leary, T. F. Changes in psychoneurotic patients with and without psychotherapy. J. Consult. Psychol., **19,** 239–245, 1955.
2. Brady, J. P., Zeller, W. W. and Reznikoff, M. Attitudinal Factors Influencing Outcome of Treatment of Hospitalized Psychiatric Patients. J. Clin. & Exper. Psychopath. In press.
3. Dymond, R. F. Adjustment changes in the absense of psychotherapy. J. Consult. Psychol., **19,** 103–107, 1955.
4. Gliedman, L. H., Nash, E. H., Jr., Imber, S. D., Stone, A. R. and Frank, J. D. Reduction of symptoms by pharmacologically inert substances and by short-term psychotherapy. A.M.A. Arch. Neurol. & Psychiat., **79:** 345–351, 1958.
5. Gliedman, L. H., Stone, A. R., Frank, J. D., Nash, E., Jr. and Imber, S. D. Incentives for treatment related to remaining or improving in psychotherapy. Am. J. Psychotherapy, **11,** 589–598, 1957.
6. Murray, H. A. *Thematic Apperception Test (and Manual)*, 3rd rev. Harvard Univ. Press, Cambridge, Mass., 1943.
7. Reznikoff, M., Brady, J. P. and Zeller, W. W. The Psychiatric Attitudes Battery: A procedure for assessing attitudes toward psychiatric treatment and hospitals. J. Clin. Psychol., **15,** 260–265, 1959.
8. Rosenthal, D. and Frank, J. D. Psychotherapy and the placebo effect. Psychol. Bull., **53,** 294–302, 1956.
9. Tougas, R. R. Ethnocentrism as a limiting factor in verbal therapy. In *Psychotherapy and Personality Change*, Rogers, C. R. and Dymond, R. F., eds., pp. 196–214. Univ. of Chicago Press, Chicago, 1954.

THE USE OF METHYPRYLON AS AN AID IN OBTAINING ELECTROENCEPHALOGRAMS IN ALCOHOLICS

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The majority of alcoholics show abnormal electroencephalograms (EEGs) during the acute phase of their illness. Most of those who are not chronic drinkers of long standing and many of those who are will show normal EEGs once the effects of the alcohol have worn off. When these patients appear for treatment, EEG readings taken at the outset and during the course of treatment furnish an aid in the diagnosis and prognosis of the disease. If abnormal EEGs are continually recorded there is good evidence that organic brain changes have occurred in the cerebral cortex. In a study of 95 alcoholics 77.4 per cent showed abnormal EEGs on the initial reading taken during the acute brain syndrome or immediately thereafter. Persistent fast or slow activity or spike discharges are more frequent in chronic alcoholic deterioration, Korsakoff's psychosis or in patients with convulsive disorders (1). The earliest change in the EEG during delirium was observed to be a general decrease in frequency, with a shift of frequency distribution spectrums to the lower range. The early changes were not associated with any striking change in regularity (3). In an experimental study of subjects who were purposely inebriated it was shown that individuals will become stabilized on a high uniform daily ingestion of alcohol. Signs of early intoxication disappeared and EEG readings reverted toward normal. Only a slight increase in the alcohol consumption, however, was necessary to unbalance the patient again (11). Knowledge of an underlying brain damage in alcoholics is an aid in psychotherapy of these patients. All too often psychiatrists treat the personality disorder without considering that the character changes may be due to brain damage (1).

Since EEG recordings are of value in diagnosing the possibility of chronic brain syndrome in alcoholic patients, it would appear to be valuable as a routine procedure for all such patients admitted to the alcoholic wards of the hospital. The chief problem there is to quiet or sedate the patient sufficiently to obtain a reading. Violent patients are often treated by aliphatic depressants such as chloral hydrate, paraldehyde or barbiturates or by anti-anxiety agents such a chlorpromazine. These agents have potentiating or synergistic effects on alcohol (9). For sedation of alcoholics they may be required in such large doses that depression of the cortex results (4) (Figure 1). The barbiturates and meprobamate have a distinct effect on the EEG (2, 6) and chlorpromazine a questionable effect (8, 10). If used for sedation to obtain EEG readings the waves produced by such sedatives would tend to complicate the picture.

Methyprylon,[2] a mild non-barbiturate sedative and hypnotic drug, does not modify the EEG while the patient is awake and the sleep tracing differs little from that of physiological sleep (14). While in one study on rats methyprylon was found to enhance the effect of alcohol (5), a study on human volunteers showed no potentiation of alcoholic excitement by methyprylon (7). In a previous study we used methyprylon to induce sleep for pediatric electroencephalography and found it to be satisfactory for this purpose. It did not generally produce fast activity although it did appear to enhance fast

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[2] Noludar: brand name of methyprylon, supplied by Hoffmann-La Roche Inc., Nutley, New Jersey.

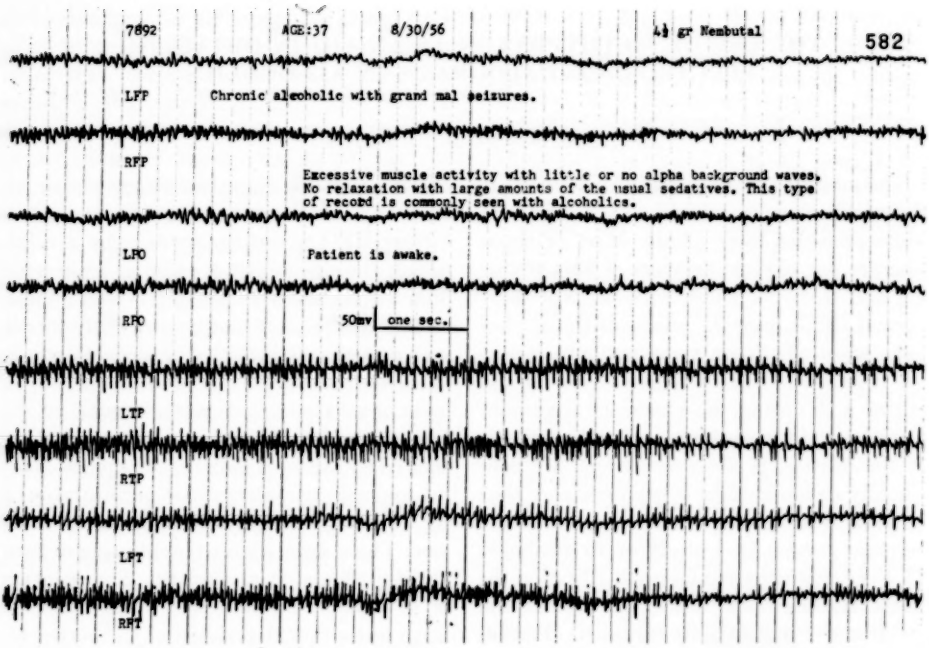

FIG. 1. Fragment of EEG record of alcoholic patient treated with Nembutal.

waves already present. From that study it appeared unlikely that methyprylon could be considered a depressant of abnormal brain wave activity and no significant side effects were noted. (12). In another study the writer determined sleep spindles can be of value diagnostically (13).

The effects of methyprylon have been observed during the sedation of alcoholic and/or drug addiction patients sufficiently to obtain EEG readings (Figure 2). In addition to the degenerative effects of chronic alcohol ingestion on the brain many alcoholics have accidents while in a state of acute inebriation. These injuries are often apparent but many of them go unnoticed.

MATERIALS AND METHODS

Eighty-two patients ranging in age between 22 and 69 years were studied in this series. Seventy-five of these were alcoholics, six drug addicts as well as alcoholics and one was a drug addict but not an alcoholic. Sixteen patients were taking sedatives. Central nervous system symptoms were discernible in 49 and included convulsive disorders, organic brain syndrome, head injury, syncope, etc. (Table 1).

The first 23 patients (Group I) were given an initial dose of 600 mg. of methyprylon and another 400 mg. in about 30 minutes if they did not appear sleepy. The remaining 59 patients (Group II) received 800 mg. as the initial dose and 400 mg. additional if within about 30 minutes they did not appear sleepy.

Length of time for induction of sleep was recorded and EEG interpretations were made.

RESULTS

In Group I, 11 patients were sufficiently sedated for the EEG recording on the first dose of 600 mg. and 12 required a subsequent dose. Nine (40 per cent) of the 11 slept within an average of 28 minutes with a range of 21 to 41 minutes. Seven (30 per cent) of the 12

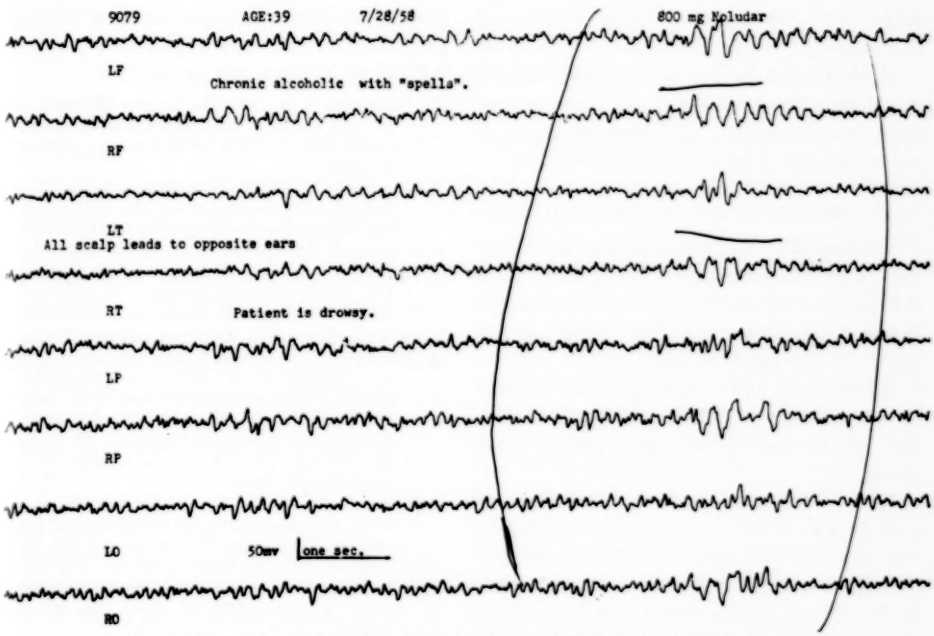

FIG. 2. Fragment of EEG record of alcoholic patient treated with Noludar.

patients who received a total dose of 1000 mg. of methyprylon slept within an average of 60 minutes with a range of 41 to 88 minutes. Two patients receiving the single dose and five receiving two doses (30 per cent) did not sleep following methyprylon administration but were sufficiently sedated for EEG records to be made. Two of four patients who showed fast activity were receiving sedatives.

In Group II, 27 patients (46 per cent) were sufficiently sedated on the first dose of 800 mg. of methyprylon. The average time of induction of sleep was 30 minutes with a range of 20 to 45 minutes. Twenty (34 per cent) of 32 patients receiving a total of 1200 mg. slept within an average of 63 minutes with a range of 35 to 127 minutes. The remaining 12 (20 per cent) who received the two doses did not sleep in an average of 75 minutes. Eight of 13 patients exhibiting fast activity were receiving sedatives.

Of the 49 patients manifesting central nervous system symptoms 29 had abnormal EEGs and 20 normal. Of the 33 patients who had no manifest symptoms 14 had abnormal EEGs and 19 normal. Four of the abnormal

TABLE 1

Condition of Patients Prior to Electroencephalograms and Results

Central Nervous System Symptoms	No. of Patients	EEG Reading	
		Normal	Abnormal
Convulsive disorder	19	8	11
Head injury	10	4	6
Head injury and convulsive disorder	6	1	5
Organic brain syndrome	6	2	4
Syncope	6	4	2
Vascular disease	1	—	1
Cerebral vascular accident	1	1	—
Totals	49	20	29
None	33	19	14
Totals	82	39	43

EEGs were considered so solely by virtue of fast activity.

Methyprylon did not appear to potentiate or enhance the alcoholic state; there was no apparent depression of blood pressure or pulse rate noted following administration.

SUMMARY AND CONCLUSIONS

Methyprylon was administered as a sedative to 82 alcoholics and/or drug addicts for the purpose of obtaining electroencephalograms. Initial doses were 600 or 800 mg. followed by 400 mg. if needed.

Satisfactory EEG readings were obtained on all patients. No untoward effects due to the administration of methyprylon were noted.

Six per cent more patients slept following a single dose of 800 mg. than after 600 mg. of methyprylon although the average time of induction of sleep was two minutes longer in the 800 mg. group. Sleep was achieved in a total of 10 per cent more patients in the group receiving 800 mg. initially than in that receiving 600 mg., indicating that the higher dosage schedule is preferable. Although 30 and 20 per cent of the patients in Groups I and II, respectively, did not sleep during the EEG, they were sufficiently cooperative and sedated to obtain satisfactory graphs.

In comparing the results with methyprylon with those of other drugs used by us for sedating alcoholic patients, we feel that methyprylon produced sleep in a higher percentage of patients than the other sedatives and that when sleep was not obtained, the records were still technically superior than has been our experience with other drugs. The sleep induced by methyprylon was obtained in a reasonable length of time. Fast activity was seen infrequently in the records. It was seen in 17 patients of whom 10 were taking other sedatives known to introduce drug-activated fast activity in the records.

In view of the favorable reaction of alcoholics to the use of methyprylon for EEGs, it may well be that this would prove to be a useful psychosedative for the therapy of such patients during treatment for their alcoholism.

REFERENCES

1. Bennett, A. E., Doi, L. T. and Mowery, G. L. The value of electroencephalography in alcoholism. J. Nerv. & Ment. Dis., **124:** 27–32, 1956.
2. Brazier, M. A. B. and Finesinger, J. E. Action of barbiturates on the cerebral cortex. Electroencephalographic studies. Arch. Neurol. & Psychiat., **53:** 51–58, 1945.
3. Engel, G. L. and Rosenbaum, M. Delirium III. Electroencephalographic changes associated with acute alcoholic intoxication. Arch. Neurol. & Psychiat., **53:** 44–50, 1945.
4. Fazekas, J. F., Shea, J. G., Sullivan, P. D. and Alman, R. W. Selective symptomatic effects of pharmacological agents in alcohol withdrawal syndromes. In *Alcoholism: Basic Aspects and Treatment*, Himwich, H. E., ed., pp. 125–132. Am. A. Advancement of Sc., Washington, 1957.
5. Graham, R. C. B., Lu, F. C. and Allmark, M. G. Combined effect of tranquilizing drugs and alcohol on rats. Fed. Proc., **16:** 302, 1957.
6. Henry, C. E. and Obrist, W. D. The effect of meprobamate on the electroencephalogram. J. Nerv. & Ment. Dis., **126:** 268–271, 1958.
7. Hoffer, A. Lack of potentiation of alcoholic excitement by methyprylon (Noludar). Canad. M. A. J., **79:** 191, 217, 1958.
8. Jorgensen, R. S. and Wulff, M. H. The effect of orally administered chlorpromazine on the electroencephalogram in man. Electroencephalog. & Clin. Neurophysiol., **10:** 325–329, 1958.
9. Koppanyi, T. Treatment of acute alcoholic poisoning. In *Alcoholism: Basic Aspects and Treatment*, Himwich, H. E., ed., pp. 93–113. Am. A. Advancement of Sc., Washington, 1957.
10. Mazzia, V. D. B., Poznak, A. V. and Artusio, J. F., Jr. Cortical effect of alphaprodine and of chlorpromazine during thiopental narcosis. J.A.M.A., **164:** 270–273, 1957.
11. Wikler, A., Pescor, F. T., Fraser, H. F. and Isbell, H. Electroencephalographic changes associated with chronic alcoholic intoxication and the alcohol abstinence syndrome. Am. J. Psychiat., **113:** 106–114, 1956.
12. Winfield, D. L. and Hughes, J. G. The use of Noludar in pediatric electroencephalography. Electroencephalog. & Clin. Neurophysiol., **9:** 713–715, 1957.
13. Winfield, D. L., Hughes, J. G. and Sayle, W. E. Electroencephalography—sleep findings in cerebral palsy. Pediatrics, **16:** 88–92, 1955.
14. Zamparo, D. Aspetti elettrooncefalografici del sonno indotto in soggetti psichiatrici con un nuovo ipnotico piperidinico. Gazzetta med. ital., **115:** 324–327, 1956.

PERCEPTUAL AND PERCEPTUAL-MOTOR DISSOCIATION IN BRAIN-DAMAGED PATIENTS

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INTRODUCTION

In previous discussions (1) and in practical clinical activity there has been a frequently made assumption that failure in block design reproduction reflects the perceptual inadequacy of the brain-damaged patient. Thus, Wechsler (3, p. 93) reports that, "among examiner's comments on the test we find the following: 'The test involves the ability to perceive forms and to analyze these forms.' 'It involves the ability to perceive pattern.' " In clinical usage, independently of what modification (2) of the Kohs blocks is used the attention of the examiner tends to be directed, at least in part, toward interpreting failure in block design reproduction as a sound measure of perceptual deficit. This practice is pursued even though it is widely recognized that many other psychological parameters may be involved in block design failure. However, even cursory inspection of the demands made on the patient by the task makes it apparent that while it is possible for perceptual inadequacy to underlie defective performance, the task itself represents more a demand for the organization of sequential action patterns in such a way that the end result approximates a perceptual model, than it does a test of perceptual adequacy itself. Interpretation of block design reproduction failure as a perceptual measure, therefore, involves a convention of clinical usage rather than a substantiated fact. Failures may stem not only from perceptual inadequacies but also from a disorganization of cerebral functioning that operates to make ineffective the determination of a voluntary action pattern even when appropriately organized perception exists. In brief, it is possible that difficulties in block design reproduction may be more sensitive indicators of apraxia than of explicit perceptual disorganization. If this is indeed the case it would follow that failures in block design reproduction often be unaccompanied by difficulties in the appropriate perception of the presented model.

The present investigation is an attempt to test the hypothesis that failure in block design reproduction is not based upon an inability correctly to perceive the model. Rather, it represents a disturbance at another level of function, namely, the inability to base the organization of sequential actions upon that which is correctly perceived.

PROCEDURES

The block design subtest of the Wechsler-Bellevue Intelligence Scale, Form I, was administered to each patient with the following procedure:

1. Time limits of the Wechsler test were adhered to except when subjects:
   (a) verbally expressed a desire to continue,
   (b) indicated by actions that they wanted to continue,
   (c) appeared to be close to solution of the task.

When any of these circumstances occurred a time extension was allowed up to a time limit of three minutes for all designs except design 7 which was allowed an extension up to five minutes.

2. Testing was discontinued when patient failed on three consecutive tasks.

3. In each case when failure was recorded and where a reproduction was offered, the patient was asked if he thought

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his reproduction looked like the model. Regardless of the verbal response the reproduction offered was copied by the examiner.

4. If the block design reproductions were obviously in disarray or not clearly offered as reproduction they were not copied by the examiner.

After the patient had failed three consecutive tasks he was presented with the card representing the model of each of these tasks together with actual block designs one of which was an accurate copy of the model, and the others of which represented erroneous copies. The models presented were constructed by the examiner outside the patient's vision (behind a screen) and consisted of: 1) a correct reproduction, 2) the patient's own originally offered solution (if he offered one) and 3) an experimentally altered reproduction previously designed by the examiner. The sub-

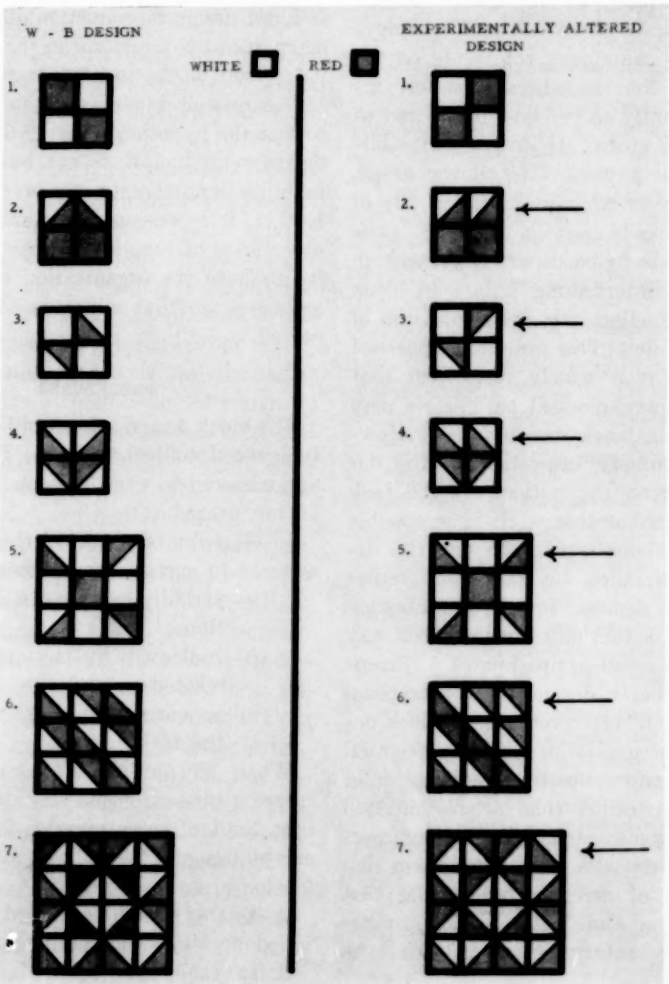

FIG. 1. Block designs, Wechsler-Bellevue Intelligence Scale, Form I, and experimental alterations.

TABLE 1
Patient Characteristics

	Age	Illness	Time Since Cerebral Accident	Wechsler Mean I. Q.		
				Verbal	Perform.	Full Scale
Non-Hemiplegics	51–85 yrs. M = 67	Diabetic or Arteriosclerotic Amputees, Hip Fracture, Arthritis	—	93	96	91
Left Hemiplegics	42–80 M = 61	Cerebral Vascular Accident	M = 3.3 yrs.	82	75	76
Right Hemiplegics	52–83 M = 63	Cerebral Vascular Accident	M = 5.6 yrs.	96*	91	91*

* Based on only six patients. Remaining four were aphasic.

jects were then asked, "Which one of these block designs looks exactly like the design on the card?"

The experimental alterations for each design are presented in Figure 1. As may be noted, block design 1 reversed the positions of red and white. In all the remaining designs the upper right corner block was rotated through 90° or 180° either clockwise or counterclockwise. It can readily be seen from Figure 1 that except for the first design, all experimental alterations were changes that involved a simple rotation of one block in the upper right corner.

The choices were presented simultaneously and in random positions so that no systematic positional preference could operate advantageously. The choices were recorded and the response time for making a choice was noted to the nearest second. The subjects used in the study are described in Table 1.

TABLE 2
Non-Hemiplegic Patients

No. Failed	No. of Originally Failed Items that were Correctly Identified	Source of Items Incorrectly Identified	
		Own Reconstruction	Altered Experimentally
3	3	0	0
2	2	0	0
3	3	0	0
3	3	0	0
3	1	2	0
3	3	0	0
3	3	0	0
3	3	0	0
2	2	0	0
3	3	0	0

RESULTS

When the 30 patients are viewed as a whole it is found that a total of 86 failures in block design copying occurred. When given the opportunity to choose the correct reproduction of block designs, the patients tested were able to make correct choices in 70 of the 86 previously failed instances. Thus, in 81 per cent of the cases the inability to make an accurate reproduction was accompanied by the ability accurately to perceive and designate a correct reproduction. It is to be noted that for the group as a whole, there were only 16 instances in which inability to reproduce the block design pattern was accompanied by the inability to make correct perceptual choices. Of these, ten errors indicated a preference for the experimentally altered pattern and six for the individual's "own" erroneous reproduction.

When the performance of each of the subgroups of patients is considered separately (Tables 2, 3, and 4) it is found that the non-hemiplegic patients exhibit the greatest intactness of perception in relation to block design reproduction failure. These patients (Table 2) failed to reproduce a total of 28 designs. However, when confronted with true and incorrect

TABLE 3
Left Hemiplegic Patients

No. Failed	No. of Originally Failed Items that were Correctly Identified	Source of Items Incorrectly Identified	
		Own Reconstruction	Altered Experimentally
4	4	0	0
3	1	0	2
3	0	0	3
3	3	0	0
3	0	2	1
3	3	0	0
3	3	0	0
3	3	0	0
3	1	0	2
3	3	0	0

TABLE 4
Right Hemiplegic Patients

No. Failed	No. of Originally Failed Items that were Correctly Identified	Source of Items Incorrectly Identified	
		Own Reconstruction	Altered Experimentally
3	3	0	0
4	3	0	1
3	3	0	0
2	2	0	0
0	0	0	0
3	3	0	0
3	2	1	0
3	2	0	1
3	3	0	0
3	2	1	0

reproductions they were able to make correct visual descriminations in all but two instances and achieved a 93 per cent level of accuracy. In only two instances was a failure to make a correct visual choice recorded. Both these failures were made by the same patient and in each instance she chose her own faulty reproduction in preference to the true or systematically altered models.

The left hemiplegic group exhibited the greatest frequency of perceptual misidentification of block designs which had been failed on initial testing. As may be seen in Table 3 correct perceptual choices were made in only 68 per cent of the trials. Two of the subjects failed to make any correct perceptual choices and four subjects made at least one error of choice.

The right hemiplegic patients in this sample performed in a manner which very closely resembled that of the non-hemiplegic group. As may be seen from Table 4 these subjects were able to make correct perceptual choices in 85 per cent of the trials. It is interesting to note that although erroneous choices were made by four individuals no subject made more than one error in perceptual identification.

When attention is directed toward the character of errors in visual choice it is found that no non-hemiplegic subject ever chose an experimentally altered pattern as correct. Two of the right hemiplegic patients identified an experimentally altered pattern as correct and two identified an "own" erroneous reproduction as correct. The left hemiplegic patients in most instances of erroneous choice exhibited a preference for experimentally altered patterns. In the ten errors of choice made by the left hemiplegic subjects eight choices of experimentally altered patterns were made. Each of the four left hemiplegic patients who made errors of perceptual choice chose at least one experimentally altered pattern.

In the sample of 30 patients studied we have found no systematic relationship to exist between I.Q. of the patient and the discrepancy between his ability to perceive designs as contrasted with his ability to reproduce them accurately.

DISCUSSION

The findings of this study demonstrate that the inability of brain-injured patients to reproduce block designs is not based upon an inability to accurately perceive the presented model. Rather, the difficulty appears to involve an inability to translate a percept into an appropriately organized pattern of acts. The ability to perceive and the inability to reproduce that which is perceived may be viewed as an instance of a more general relation between stages

of ontogenetic development and the vulnerability to brain damage.

It is widely recognized that discrimination of forms or objects is achieved at an earlier age than is the ability to reproduce them. At year IV in Form L of the revision of the Stanford-Binet test of intelligence the child is expected to identify correctly of 10 different geometric forms offered. Yet, not until year V is he expected to accurately reproduce a simple square. Another example of this explicit, clinical recognition of the developmental hierarchy of brain function, developed theoretically by Hughlings Jackson, is the fact that at year II the child is expected to identify parts of the body on a paper doll, but he is not expected to complete the drawing of an incomplete man until he is aged IV. In conjunction with this recognition, and in a somewhat different area, it is appropriate to point out that aphasic patients who premorbidly spoke two or more languages, are often found to retain greater portions of their native tongue while losing greater portions of their second language. Thus, the effects of brain injury on behavior appear to follow a general law of ontogenetic stability, whereby earlier learned functions are less affected by neurologic damage than are more recently acquired patterns. In accordance with this postulate, it is not surprising that brain injured patients do more poorly at a task requiring them to reproduce a complex design than they do at discriminating one design from another. However, perhaps more important than the finding in this study, that they do indeed discriminate designs better than reproduce them, is the implication that we are dealing with functionally autonomous systems—a perceptual system which develops earlier and a perceptual-motor or action system which develops later and is more vulnerable to central nervous system damage. In any event, it appears to be necessary in discussing perceptual tasks to differentiate the discriminative perceptual function from the perceptual-motor. It should be clear, therefore, that perceptual motor inadequacy, *per se*, does not permit the inference of perceptual disturbance. Perceptual-motor dysfunctions are probably more relevant as indicators of apractic disorders.

SUMMARY

The block design subtest of the Wechsler-Bellevue Intelligence Scale, Form I, was administered to ten left hemiplegic patients, ten right hemiplegic patients and ten patients with no known central nervous system injury. After an initial sequence in which the patient demonstrated his ability to reproduce the designs, the patient was then asked to choose from actual block models that model which looked exactly like the card containing the representation of the block design.

Among the 30 patients tested, there were a total of 86 failures in block design reproduction. When confronted with the opportunity to make a discriminating choice of block designs as related to a model, the patients were able to choose the correct design in 70 of the 86 instances. Implications are drawn from these results for the concept of levels of ontogenetic vulnerability in brain-damage, and for a consideration of perceptual-motor as differentiated from perceptual functioning.

REFERENCES

1. Goldstein, K. and Scheerer, M. Abstract and concrete behavior; an experimental study with special test. Psychol. Monogr., **53**: No. 2, 1941.
2. Nadel, A. B. A qualitative analysis of behavior following cerebral lesions. Arch. Psychol., No. 224, 1938.
3. Wechsler, D. *The Measurement of Adult Intelligence*, 3rd. ed. Williams & Wilkins, Baltimore, 1944.

A STUDY OF LACTIC DEHYDROGENASE ACTIVITY OF CEREBROSPINAL FLUID[1]

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The assays of certain enzyme activities have been used as an aid in making specific clinical diagnoses. Most of these procedures have been done on blood, plasma or serum because of their availability. In almost every hospital the list of such determinations now in daily use is steadily growing. Recently the transaminases have been shown to be of great help in the diagnosis of certain cardiac and muscular disorders; and in the last six to twelve months a number of publications concerning lactic dehydrogenase activity in biological fluids have appeared.

It is the purpose of this paper to review briefly the recent work of medical interest concerning lactic dehydrogenase and to note specifically its presence and behavior in one biological fluid (cerebrospinal fluid) as compared to the enzyme (or enzymes) found in serum. That this distinction is important is seen from the recent demonstration that three separable proteins have lactic dehydrogenase activity in serum (31) and that serum lactic dehydrogenase and muscle lactic dehydrogenase have different types of maximum activity curves with DPNH and pyruvate (29). It has even been shown that different crystalline lactic dehydrogenase preparations from the same source can behave variably (29). There are also differences between lactic dehydrogenase obtained from different organs in one species as well as species differences (26).

Lactic dehydrogenase is present in plant, bacteria, yeast and animal tissue. It is now fairly well established that the enzyme found in the plant, bacteria and yeast differs in its behavior from that obtained in animal tissue (7), as it does not require a pyridine nucleotide coenzyme (2) and it has different pH characteristics. The following discussion deals with lactic dehydrogenase of animal origin.

This enzyme has usually been prepared in crystalline form from rabbit muscle (13) and pig heart (22) by the method of Straub (28). Both preparations seem to behave similarly for the most part. Activity has been demonstrated in many animal tissues; specifically, in humans, it has been shown in heart, liver, muscle, kidney, spleen, lung, pancreas, serum and cerebrospinal fluid (35, 36, 37). It requires a coenzyme of the pyridine nucleotide family. DPNH is approximately 100 × −380 × more active than TPNH (16, 17). It catalyzes the reaction of lactic acid → pyruvic acid; but Meister notes that the crystalline enzyme will also reduce α ketobutyrate, α ketovalerate, α ketocaproate and phenylpyruvate but not oxaloacetate, α ketoglutarate and other B keto acids (19). It only acts on the l (-) form of lactic acid (24).

The assay is usually carried out by noting the rate of appearance or disappearance of DPNH at 340 mμ under standard conditions. As is true with other pyridine nucleotide enzymes the rate is more rapid when DPNH rather than DPN is used as one of the substrates. The enzyme is quite stable and will last for months at 3° to minus 15° C. The assay with reduced DPN is routinely carried out at pH 10.0. The reverse reaction is usually studied at pH 7.0.

The molecular weight is approximately

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135,000 (22). In most crystalline preparations there is a single boundary in the ultracentrifuge, but usually two fractions are noted in salting procedures and electrophoresis. These have been called the A (anode) and C (cathode) fractions (18, 22, 23). The sedimentation constant S_{20} has been noted to be 6.48 and 6.36 $\times$ 10^{-13} seconds. The free diffusion constant D_{20} was 5.3 $\times$ 10^{-7} cm^2 per second for fraction A (25). Both fractions precipitate below pH 4.5. The iso-electric points 4.5 and 4.8 have been estimated for fractions A and C respectively. Turnover numbers are 12,800 and 8150 moles substrate per minute at 25° C per 135,000 gm. of protein (22) and 37.000 at pH 7.0 with DPNH (24). The reported Km values for pyruvate are 1.7 $\times$ 10^{-5} and 5.2 $\times$ 10^{-5} M.

Vallee has shown this enzyme to contain zinc and to be a true metalloenzyme (30). Its behavior with inhibitors is similar to other metalloenzymes.

A definite enzyme substrate complex has been demonstrated (5, 6); the enzymes' active site has a similar sterochemical specificity to the active site of yeast alcohol dehydrogenase (15).

CLINICAL DATA

Lactic dehydrogenase activity was reported in serum by Wacker *et al.* (32), who gave as a normal value 59 $\pm$ 19 units (a unit defined as a change of 0.001 in Optic Density per minute). They pointed out that there was a rise in enzymatic activity after myocardial infarction and suggested its possible use as a clinical test. They also noted its elevation in cirrhosis and renal necrosis. Numerous papers confirming these findings in humans have been published (1, 9, 14, 36). There is some evidence to suggest that the degree of rise may be proportional to the size of the myocardial infarction. In humans the elevation is usually noted within six to 12 hours, and reaches its peak in 24 to 48 hours (35). Experimental observations in dogs, where myocardial ischemia is produced by ligation of vessels, demonstrated that following infarction there was no change of enzyme activity in heart muscle extract for two hours. Then there was a rapid fall to 30 to 50 per cent of normal within 15 hours (12).

Its presence in elevated amounts in liver disease has been confirmed (11). It has been looked for in patients with cancer (10), and found to be only of limited value. In some patients with active muscular disease it has been found to be elevated (8).

Lactic dehydrogenase was first demonstrated in cerebrospinal fluid by Scheller (27) and Bruns (4). The presence of elevated lactic dehydrogenase activity in cerebrospinal fluid was noted in some patients by Fleischer *et al.* (8). (Preliminary studies with cerebral infarctions in dogs had given elevated values, although no data were published.) Cerebrospinal fluid lactic dehydrogenase activity was about 17 per cent of serum activity. These investigators concluded that elevated findings were seen in head injury, degenerative disease and convulsive disorders. There was no change seen in patients with tumor. These findings were not confirmed by Wróblewski *et al.* (37, 38), in another study done with this enzyme. They noted elevations of enzyme activity with meningitis, leukemia, lymphoma and metastatic carcinoma, but not in degenerative disease.

Studies with other enzymes in cerebrospinal fluid, *i.e.*, cholesterase, ali-esterase (8, 20), transaminase (3) have also been undertaken.

Our interest in the possible diagnostic use of these enzymes was aroused because of the reported correlation of transaminases in cerebrospinal fluid with brain damage (8, 20). Lactic dehydrogenase is present in abundant amount in brain tissue, and it was thought that the blood-brain barrier probably would make serum determinations of this enzyme meaningless. Any rational investigation would have to ex-

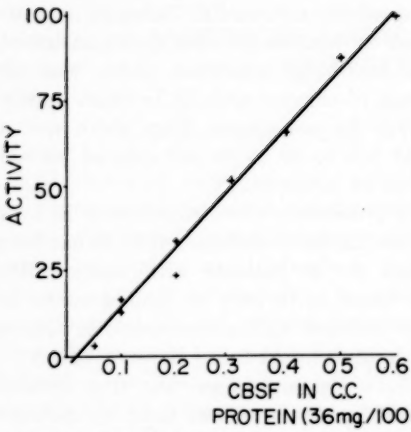

FIG. 1. The effects of increasing amounts of cerebrospinal fluid from a single patient on the Lactic Dehydrogenase Assay. (All activities are measured in optic density units × 1000 per minute, unless otherwise noted.)

amine the biological fluid in immediate proximity to brain substance, *i.e.*, cerebrospinal fluid. Preliminary study quickly demonstrated that serum lactic dehydrogenase activity does not get into the cerebrospinal fluid, and there was little a priori reason to expect otherwise.

Since the effect of cerebrospinal fluid has never been determined on the assay system, our first problem was to go through the various procedures to decide on a suitable assay system and, second, to try to determine if the enzyme behaved the same in blood and cerebrospinal fluid (since it arises from different tissues).

MATERIAL AND METHODS

Cerebrospinal fluid was obtained from normal people undergoing surgery and requiring spinal anesthesia. A variety of abnormal cerebrospinal fluids were obtained during the course of diagnostic testing in the medical wards and in various neurosurgical procedures. The various experiments were done on large pooled samples of cerebrospinal fluids until the conditions of assay were set up. Absorption at 340 mμ was measured on a "coenzometer" (Macalaster Bicknell). A unit of activity was defined as a change in Optic Density of 0.001 in one minute at room temperature (24° C).

EXPERIMENTAL RESULTS

EFFECT OF AMOUNT OF CEREBROSPINAL FLUID

Increasing amounts of cerebrospinal fluid will give a linear increase in activity under the conditions of assay. This is true of the reaction measured in both directions. Approximately 2 to 3 × the activity was noted when the reaction was studied in the direction Pyruvate + DPNH → Lactic acid + DPN. Assays with varying amounts of cerebrospinal fluid are shown in Figure 1. Different spinal fluids show different activities and there is no direct relationship of activity to either volume or protein content of two cerebrospinal fluid samples from two individuals. The specific spinal fluid shown in Figure 1 was an unusually active specimen. Amounts of cerebrospinal fluid greater than 1.0 cc are impractical because of the difficulty in obtaining large amounts in any given patient and the limitations of volume of the assay system.

STUDY OF THE BACK REACTION

DPN + Lactic acid → Pyruvate + DPNH

The most active assays were all at higher pH. Figure 2 presents a number of assays, and it is to be noted that pH greater than 9.5 had to be obtained for optimal activity. A curve of this type suggests that an H^+

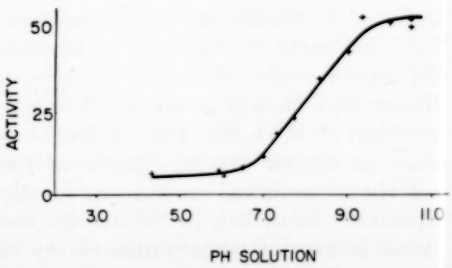

FIG. 2. The effects of pH on the assay of Lactic Dehydrogenase, using DPN as the substrate.

may have occupied an active site of the enzyme or coenzyme and needed to be removed before a reaction could be initiated.

Figure 3 shows the response to temperature. There is a fairly good increase with rising temperature to about 45° C., and then there is less activity and a gradual fall. This temperature optimal is slightly lower than that seen for many other enzymes in pure state.

Maximal DPN effect was seen at concentration about 1.0×10^{-3} M. solution. A final concentration of 5.0×10^{-5} M. solution had to be achieved before any significant amount of reaction took place under the experimental conditions (Figure 4).

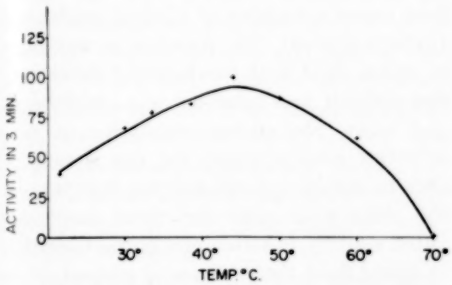

FIG. 3. The effects of temperature on Lactic Dehydrogenase activity of cerebrospinal fluid. The peak occurs at a lower temperature than that seen with pure enzyme.

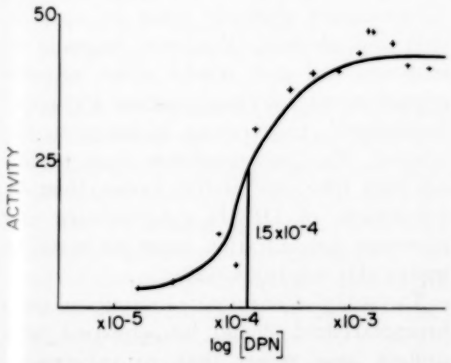

FIG. 4. The effect of varying concentrations of DPN on the activity of Lactic Dehydrogenase in cerebrospinal fluid. The experimental Km (½ V max) is 1.5×10^{-4}.

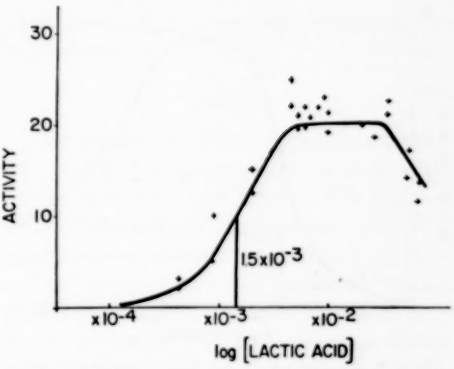

FIG. 5. Activity of Lactic Dehydrogenase with varying concentrations of lactic acid as substrate. The experimental Km (½ V max) was 1.5×10^{-3}.

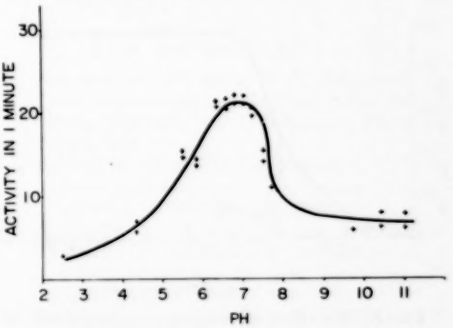

FIG. 6. The activity of the forward reaction when pH is varied. A very sharp optimum is noted in cerebrospinal fluid.

Lactic acid concentration between 4.0×10^{-3} and 4.0×10^{-2} M. solution gave maximal enzyme activity. At higher values (greater than 10^{-1} M.) there was a decreasing activity with increased molarity (Figure 5).

FORWARD REACTION

The optimal pH was between 6.5 and 7.4. There was a sharp decrease in activity on both sides of this point (Figure 6).

Pyruvate concentration showed a maximal activity at about 3.0×10^{-4} M. to 1.0×10^{-3} M. range and a progressive inhibition above this concentration (Figure 7).

DPNH must be present in at least 1×10^{-5} concentration to see any significant

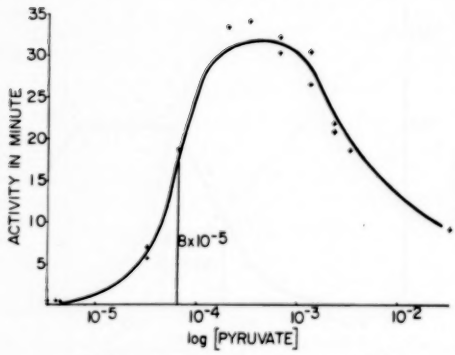

FIG. 7. The effect of varying concentrations of pyruvate on the activity of cerebrospinal fluid Lactic Dehydrogenase. The experimental Km is 8.0×10^{-5}.

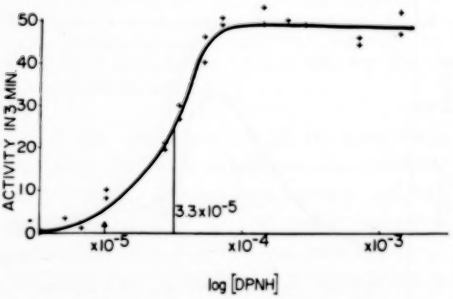

FIG. 8. The effect of varying concentrations of DPNH on the enzyme activity. The experimental Km is 3.3×10^{-5}.

reaction under the conditions in which the enzyme activity was measured. Between 8×10^{-4} and 2×10^{-2} the maximal effect of DPNH is seen and there was little change as concentrations were increased up to 1.0×10^{-2} M. solutions (the highest it was practical to measure). These are plotted in Figure 8.

DISCUSSION

An assay for lactic dehydrogenase can be run using either the forward or the back reaction. Because of the low intrinsic activity in most samples of spinal fluid the forward reaction is more desirable since it yields a higher measurement. Preincubation is necessary, as there is ordinarily some pyruvate and lactate present in most cerebrospinal fluids. As pyruvate concentration is critical this must be removed before the reaction begins.

As in all assays for enzymes, temperature control is exceedingly important and the conditions of assay must be standardized and specified. The failure to do this has made many of the results of studies of enzymatic activity in various clinical situations difficult to reproduce.

On the basis of behavior of cerebrospinal fluid lactic dehydrogenase activity it was felt that there was a great similarity between lactic dehydrogenase activity in serum and cerebrospinal fluid. An enzyme assay system using the forward reaction was selected for future investigation of the presence of this enzyme in cerebrospinal fluid under a number of clinical conditions (to be reported). The presence of anything in spinal fluid that would make investigation difficult was ruled out, *e.g.*, inhibitors; and under the chosen conditions of pH, substrate concentration, etc. one should be able to obtain optimal enzyme activity. In the observation that one could have elevated activity in serum and normal activity in spinal fluid, the presence of a blood-brain barrier was confirmed.

The utilization of optimal amounts of substrate and the realization that the substrate may also inhibit the reaction in some circumstances similarly must be appreciated and checked. Excessive amounts of substrate will give results which are not related to enzyme concentration. Pyruvate, particularly, may be an inhibitor to the reaction. Rate measurements must be linear with time, and if this varies, then readjustment of DPNH concentration and pyruvate concentration must be made to insure this condition (**29**).

The study of enzymatic activity on cerebrospinal fluid should be compared to a protein base rather than to volumes of cerebrospinal fluid, if possible. The vast majority of enzymatic data today is so reported. Since these figures are almost

ways available to the clinician studying cerebrospinal fluid, reporting of activity per mgm protein is vastly more desirable than activity per cc spinal fluid—especially when protein content is known to vary so much under varying clinical conditions. The method of determining protein and the standard used are also important. Albumin, the usual standard, will give different values when determined chemically by the most common procedure for spinal fluid protein and when protein is measured by an E_{280} reading (one of the more common methods of the enzymologist).

It should be emphasized that we have studied an enzyme activity in cerebrospinal fluid and not the enzyme itself. Thiers and Vallee (29) have pointed out that there are three assumptions inherent in this statement: 1) enzyme activity and enzyme concentration are simply related so concentration can be inferred from the activity; 2) enzymes defined by their activity are simple chemically homogenous entities; 3) kinetics which apply to one activity apply equally well to that same activity under different conditions.

These writers show that with lactic dehydrogenase, and almost certainly with most other enzymes, the assumptions are not strictly true. It may be that the purified enzyme might have other properties. At present an attempt to obtain purified lactic dehydrogenase from brain is being undertaken.

Little is known about the role of enzymes in cerebrospinal fluid. It is our hope that by studying a few enzymes in various types of disorders some clues may be obtained as to the mechanism of certain phenomena frequently noted in these neurological diseases. Present-day laboratory procedures use such measurements as "protein content" which are usually correlated with certain disorders by a process of memory and association. A knowledge of some of the components of this protein content may help the clinician concerned with such problems in understanding spinal fluid changes in disease states.

SUMMARY

The conditions affecting the measurement of lactic dehydrogenase activity in cerebrospinal fluid have been studied. The dependence of the activity on substrate, pH, temperature was characterized.

The enzyme activity in cerebrospinal fluid appears to behave similarly to that found in blood. The presence of a blood-brain barrier for lactic dehydrogenase activity was confirmed. A brief review of the literature pertinent to these observations was presented.

REFERENCES

1. Amelung, D., and Horn, H. D. Fermentaktivitäts-Bestimmungen im Serum beim Herzinfarkt. Deutsche med. Wchnschr., **81**: 1701–1704, 1956.
2. Bach, S. J., Dixon, M. and Zertas, L. C. Yeast lactic dehydrogenase and cytochrome B_2. Biochem. J., **40**: 229–239, 1946.
3. Bernsohn, J., Boshes, B. and Possley, L. A study of cholinesterase and aliesterase in various neurologic diseases. Neurology, **8**: 221–226, 1958.
4. Bruns, F. H., Jacob, W. and Weverinck, F. Phosphohexoisomerase, phosphoriboseisomerose and lactic acid dehydrogenase in spinal fluid. Clin. chem. acta, **1**: 63–66, 1956.
5. Chance, B. and Nielands, J. B. Studies on lactic dehydrogenase of heart. J. Biol. Chem., **199**: 383–391, 1952.
6. Chance, B. and Theorell, H. Studies on liver alcohol dehydrogenase. Acta chem. scandinav., **5**: 1127–1144, 1951.
7. Dixon, M. Lactic dehydrogenase from yeast. In *Methods in Enzymology*, Colowick, S. P. and Kaplan, N. O., eds., Vol. 1, pp. 444–449. Academic Press, New York, 1955.
8. Fleischer, G. A., Wakim, K. G. and Goldstein, N. P. Glutamic-oxaloacetic transaminase and lactic dehydrogenase in serum and cerebrospinal fluid of patients with neurological disorder. Proc. Staff Meet. Mayo Clin., **32**: 188–197, 1957.
9. Gavosta, F., Brusca, A. Distasi, M., Pileri, A. and Vergnano, F. Attivita lattico-deidrogenasica del siero in vari stati morbosi. Minerva med., **47**: 1078–1082, 1956.
10. Hill, J. H. Serum lactic dehydrogenase in cancer patients. J. Nat. Cancer Inst., **18**: 307–313, 1957.
11. Horn, H. D. and Amelung, D. Die Bedeutung von Transaminasen-und Milchsäure dehydro-

genase-Bestimmungen im Serum bei Leberkrankungen. Deutsche med. Wchnschr., **82:** 619–626, 1957.

12. Jennings, R. B., Kaltenbach, J. P. and Smetters, G. W. Enzymatic changes in acute myocardial ischemic injury. A. M. A. Arch. Path., **64:** 10–16, 1957.
13. Kornberg, A. Lactic dehydrogenase of muscle. In *Methods in Enzymology*, Colowick, S. P. and Kaplan, N. O., eds., Vol. 1, pp. 441–443. Academic Press, New York, 1955.
14. Leren, P. Interventricular septum infarction. Acta med. scandinav., **157:** 157–163, 1957.
15. Loewus, F. A., Otner, P., Fischer, H. F., Westheimer, F. H. and Vennesland, B. The enzymatic transfer of hydrogen. J. Biol. Chem., **202:** 699–716, 1953.
16. Mehler, A. H., Kornberg, A., Grisolia, S. and Ochoa, S. The specificities of some dehydrogenase toward pyridine nucleotides. Fed. Proc., **6:** 278, 1947.
17. Mehler, A. H., Kornberg, A., Grisolia, S. and Ochoa, S. The enzymatic mechanism of oxidation-reductions between malate or isocitrate and pyruvate. J. Biol. Chem., **174:** 961–977, 1948.
18. Meister, A. Reduction of alpha gamma-diketo and alpha keto acids catalyzed by muscle preparations and by crystalline lactic dehydrogenase. J. Biol. Chem., **184:** 117–129, 1950.
19. Meister, A. Crystalline lactate dehydrogenase. Biochem. Preparations, **2:** 18–22, 1952.
20. Miyazaki, M. Comparative serum and cerebrospinal transaminase levels in acute cerebrovascular disorders. Bull. School Med. Univ. Maryland, **42:** 20–26, 1957.
21. Miyazaki, M. Glutamic oxaloacetic transaminase in cerebrospinal fluid. J. Nerv. & Ment. Dis., **127:** 169–175, 1958.
22. Nielands, J. B. The purity of crystalline lactic dehydrogenase. Science, **115:** 143–144, 1952.
23. Nielands, J. B. Studies on lactic dehydrogenase of heart. II. J. Biol. Chem., **199:** 373–387, 1952.
24. Nielands, J. B. Studies on lactic dehydrogenase of heart. III. J. Biol. Chem., **208:** 225–230, 1954.
25. Nielands, J. B. Lactic dehydrogenase of heart muscle. In *Methods in Enzymology*, Colowick, S. P. and Kaplan, N. O., eds., Vol. 1, pp. 449–454. Academic Press, New York, 1955.
26. Pfleiderer, G. and Wieland, T. Nachweis der Heterogenität von Milchsäuredehydrogenasen ver schiedenen Ursprungs durch Trägerelektrophorese. Biochem. Ztschr., **329:** 112–116, 1957.
27. Scheller, R. Ueber die Milchsäuregehait des Liquor Cerebrospinales. München med. Wchnschr., **73:** 1652–1654, 1926.
28. Straub, F. B. Crystalline lactic dehydrogenase from heart muscle. Biochem. J., **34:** 483–486, 1950.
29. Thiers, R. and Vallee, B. L. Analytical consideration in serum enzyme determinations. Ann. New York Acad. Sc., **75:** 214–226, 1958.
30. Vallee, B. L. and Wacker, W. E. C. Zinc: A component of rabbit muscle lactic dehydrogenase. J. Am. Chem. Soc., **78:** 1771–1772, 1956.
31. Vessel, E. S. and Bearn, R. G. Localization of lactic acid dehydrogenase activity in serum fractions. Proc. Soc. Exper. Biol. & Med., **94:** 96–99, 1953.
32. Wacker, W. E. C., Ulmer, D. D. and Vallee, B. L. Metalloenzymes and myocardial infarction. New England J. Med., **255:** 449–456, 1956.
33. Wakim, K. G. and Fleischer, G. A. The effect of experimental cerebral infarction on transaminase activity in serum, cerebrospinal fluid and infarcted tissue. Proc. Staff Meet. Mayo Clin., **31:** 391–399, 1956.
34. White, L. P. Serum enzymes. New England J. Med., **255:** 984–988, 1956.
35. Wróblewski, F. and LaDue, J. S. Lactic dehydrogenase activity in blood. Proc. Soc. Exper. Biol. & Med., **90:** 210–213, 1955.
36. Wróblewski, F., Ringsegger, P. and LaDue, J. S. Serum lactic dehydrogenase activity in acute transmural myocardial infarction. Science, **123:** 1122–1123, 1956.
37. Wróblewski, F., Decker, B. and Wróblewski, R. Activity of lactic dehydrogenase in spinal fluid. Am. J. Clin. Path., **28:** 269–271, 1957.
38. Wróblewski, F., Decker, B. and Wróblewski, R. The clinical implications of spinal fluid lactic dehydrogenase activity. New England J. Med., **258:** 635–639, 1958.

ENURESIS: AN EMOTIONAL SYMPTOM?

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Enuresis means, plainly, emission of urine. However, it has come to imply more. The word now connotes *involuntary* emission of urine with no demonstrable organic cause and in general medical usage it is not necessarily interchangeable with "incontinence," a term usually reserved for other involuntary forms of wetting, *i.e.*, in babies, in organic brain syndromes, etc.

The application of the term enuretic, in spite of semi-specific implications, is still not standardized. Different investigators working on enuresis have not used the same criteria for delineating their enuretic population. For example, Ackerson (1) used the age of three as the cut-off, point while Healy and Bronner (11) used eight years. Therefore many of the children considered enuretics by Ackerson would never have been included in the Healy and Bronner study since some of them would have stopped wetting in the ensuing five years.

The present study is part of a larger study by the Mental Health Research Program of the St. Louis County Health Department and Washington University supported by research grant M-592 from the National Institutes of Health, U. S. Public Health Service. The sample selected for study is composed of 830 white families, each having at least one child in the third grade in one of fifteen schools located in St. Louis County.

In this study enuretics are defined as all those third graders (eight and nine year olds) who still wet the bed at least once a month. Included are 18 children who had stopped wetting for a period but have since resumed, (so-called "acquired"). Children who wet only with "regression" brought about by illness ("only when he has a cold") and those who do so "only after drinking too many fluids prior to bedtime" are considered enuretics if they have wet within the last month and have been wetting regularly. The occasional bed-wetter (less than once a month) is excluded. The homogeneity of this group is therefore founded on the premise that all the subjects are presently enuretics.

The question on enuresis appearing in the questionnaire administered to the participating families is reproduced below.

Does he (she) ever wet himself (herself) or in bed?.....

a. How often does he (she) have this trouble?.....

b. How long has he (she) had this trouble?

.....

c. How serious is it?.....

d. Does this occur at:.....Home.....

School....Both

For another part of the study, ratings of general adjustment were made by the children's teachers on a four-point rating scale. The teacher's rating was used where professional ratings by psychiatric social workers were not available. In a previous study (7) it was found that the teacher's opinion agreed exactly with the opinion of the professional mental health personnel in 86 per cent of the cases. This agrees closely with Ullman (19) who has reported an .86 correlation between clinical and teacher assessment of pupil adjustment. The adjustment categories are described as follows:

1. *Well-adjusted:* A happy child who is well adjusted in his relationships with others and in his accomplishments.

2. *No significant problems:* A child who gets along reasonably well and accomplishes reasonably well the things that usually go with his age and level of development, and may be considered normal or average.

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3. *Marginally disturbed:* A child who is not so happy as he might be; has moderate difficulties getting on; growing up represents something of a struggle.

4. *Clinically disturbed:* A child who has, or, at his present rate is likely to have, serious problems of adjustment, and needs clinical help because of such problems.

By this method of assessment, the sample of 830 included 167 well-adjusted children, 429 children with no significant problems, 166 marginally disturbed children, and 68 clinically disturbed children—thus about 28 per cent rated as with at least marginal disturbance. Six cases were eliminated from the study because of insufficient information, thus accounting for the small mathematical discrepancy.

Information about the presenting symptoms of the child was obtained in a private, home interview with the mother of the child. The mother was asked a series of questions about various characteristics of the family and the family background. Following this she was introduced to a series of questions which made up the symptoms inventory and took this form: "Does Johnny have trouble .....(eating, sleeping, getting along with other children, etc.)"? Affirmative responses were followed by probes in a) the specific nature of the difficulty, b) frequency, c) duration and d) severity. (see specific enuresis question above). This line of questioning was continued through twenty-one areas of difficulty.

The number of symptoms was defined as the number of symptoms reported by the mother. The range of possibility extended from the minimum of reporting no presenting symptoms in the child, to the maximum number of twenty-one. One hundred and twenty-nine mothers reported no symptoms; the mode was two; and only one mother reported as many as twelve symptoms.

Teachers were also asked to complete a symptom inventory with which correlations could be made.

TABLE 1

Incidence of Enuresis by Adjustment Categories

	Adjustment Category				Total
	1	2	3	4	
Total	167	425	164	68	824
Enuretic	18	36	22	7	83
Per cent	10.8	8.5	13.4	10.3	10.1

RESULTS

The results obtained in the present study will be summarized in a series of tables, and previous studies will be cited for immediate comparative purposes.

Combining categories 1 and 2 (non-disturbed) in Table 1 yields a per cent of 9.1 enuretics. This, compared with categories 3 and 4 (disturbed) combined to an average of 12.5 per cent, gives a difference of 3.4 per cent. This difference, however, is not significant by a chi-square test for distribution, using Yates' correction ($p > .20$). Note that the most disturbed group had a smaller percentage of enuretics than the best adjusted. The incidence of 10.1 per cent of enuretics for the whole group corresponds closely to Hallgren's (10) results. In a series of 2000 school children seven years of age, he found 11 per cent to be enuretic. The incidence for the four groups in the present survey, however, seems contradictory to the expected association of enuresis and emotional disturbance.

Computations were also made to determine the incidence of enuresis according to the symptoms which the mother reported. These symptoms are those commonly associated with behavior problems in children. Glidewell, Mensh, and Gildea (8) showed that a reliable, positive relationship exists between the number of symptoms as reported by mother and the degree of sickness found in the child by Child Guidance Clinic or other formal psychiatric diagnostic studies. This is not to say that "emotionality" is but an absence of symptoms which are annoying to parents and teachers, but that emotional adjustment, clinically determined,

correlates with the number of symptoms present. In other words, children with most symptoms may be expected to be more disturbed than those with a lesser number of symptoms.

It was observed that the incidence of enuresis increased with the number of symptoms (Table 2). If the enuretic cases were distributed evenly among 21 emotional symptoms, chance alone would account for 4.8 per cent of children with only one symptom to be enuretics and 33 per cent or greater of children with seven or more symptoms to be enuretics. The relationship actually seems a negative one. In the present sampling, calculations on the actual distribution of symptoms gives probabilities by chance alone of 4 per cent to 28.4 per cent.[4]

When the number of symptoms as reported by the teachers is correlated with enuretics, (see Table 3) there is, up to the 5 and 6 symptom group, no rise in the incidence of enuresis. The 20.5 per cent enuretics in the 7+ symptom group is probably an artifact of the method although it must also be considered as possibly the only figure in this study which correlates enuresis and emotional disturbance.

In about three-fourths of these cases, the teachers had no knowledge of the child's enuresis, so that it was entirely possible for her to consider a child asymptomatic who actually wet the bed at home. In fact, 8.3 per cent of the children considered by teachers to be asymptomatic were actually nocturnal enuretics. An appreciable incidence of enuresis was found in what would seem to be well-adjusted children from the point of view of absence of symptoms as seen by the teacher.

Another approach is in terms of so-called symptom constellations. Certain emotional symptoms tend to be found together in high correlation, *e.g.* lying and stealing. Occasionally significant correlations between enuresis and some other symptom is reported.

[4] The mathematical formula for this would read as follows. Example: If enuresis exists 84 times among 2067 symptoms, then among 173 children with only one symptom there would be seven enuretics or, of 173, 4 per cent.

TABLE 2

Incidence of Enuresis by Number of Symptoms As Reported by Mother

No. of Symptoms	Children	Enuretics	Per cent enuretics	% Probability by chance alone
0	128	0	0.0	—
1	173	14	8.1	4
2	181	20	11.0	8.1
3	127	18	14.2	12.2
4	83	12	14.5	16.2
5–6	84	12	14.3	22.2
7+	51	8	15.7	28.4

TABLE 3

Incidence of Enuresis by Number of Symptoms As Reported by Teacher

No. of Symptoms	Children	Enuretics	Per cent enuretics
0	193	16	8.3
1	160	10	6.25
2	123	15	12.2
3	94	9	9.6
4	67	6	8.9
5–6	80	6	7.5
7+	107	22	20.5

Table 4 presents the correlation findings of this study. In a sense, this might be considered to be looking at the other side of the coin. Since it would seem that disturbed children are not particularly enuretic, this approach is to see whether enuretic children are more disturbed, and if enuresis correlates to any degree with other symptoms.

The table is self-explanatory. In no instance does it show to any significant degree that enuretics have greater maladjustment than non-enuretics, or that enuresis correlates with any symptom better than $p = .20$ as is the case with thumbsucking.

DISCUSSION

Levin (13) found a high correlation between nightmares and enuresis in Navy men. (This, of course, is not a comparable study because it dealt in adults.) Hallgren (9)

TABLE 4

Symptom Incidence: Non-Enuretic and Enuretic Subjects

Type of symptom	Non-Enuretics (N = 698)		Enuretics (N = 83)		
	N with symptom	% with symptom	N with symptom	% with symptom	*p*
Eating	205	29.3	20	24.0	0.50
Sleep	61	8.7	4	4.8	0.50
Stomach	50	7.1	9	10.8	0.50
Fears	132	18.9	15	18.1	—
Nervousness*	217	31.0	32	38.6	0.50
Thumbsucking	57	8.2	11	13.2	0.20
Sex	13	1.9	1	1.2	—
Speech	69	9.9	5	6.0	0.50
Acting-out c. adults	43	6.1	0	0.0	—
Acting-out c. peers	60	8.6	7	8.4	—
Withdrawn c. peers	48	6.9	6	7.2	—
Lying	94	13.5	10	12.0	—
Stealing	110	15.7	0	0.0	—
Withdrawn c. adults	11	1.6	0	0.0	—

* Includes nail-biting.

found what he considered a significant correlation between enuresis and sleep disturbance in children.

Michaels and Goodman (16) found differences between enuretics and non-enuretics as to nail-biting and speech impediments to be $+12 \pm 4.0$ and $+17 \pm 5.7$ respectively (the latter figure being the standard deviation.) Hallgren (10) also correlated enuresis significantly with speech disorders and pyloric stenosis.

On the other hand, correlations reported by Ackerson (2) of enuresis and other "personality and conduct difficulties" were generally low. Bed wetting past the third year of age was considered a conduct problem and this early cut-off point (3 years) should be noted as it brought a 23 per cent rate of enuretics to the study. Nevertheless, its biserial correlation with conduct-total (where enuresis falls) was .16 and .18 for boys and girls respectively. (For this study .20 was considered the lower limit of significance.) Ackerson concluded that, "*Enuresis* in our data, therefore, appears to have little meaning other than as an annoyance in itself." It is interesting to note in this study that correlations above the index of .20 between enuresis and certain traits were usually found in girls. As an example, enuresis and nail-biting correlated to the extent of .24 and .18, for girls and boys respectively. Correlation of enuresis with police arrests, on the other hand, was .07 and −.25 for boys and girls respectively.

Anderson (3) found no correlation with thumbsucking and expressed the belief that a high incidence of nail-biters was as a result of anxiety brought on by the maladjustment arising from the enuresis itself. Anderson also concluded that the average intelligence of enuretic children was slightly above the unselected mean. This observation, incidentally, has been contradicted by other studies (2).

Gerard (6) as well as others have thought of enuresis as an expression of sexual difficulties. Among the dynamic elaborations suggested are repressed masturbation, fear of the opposite sex, desires for male potency or desire to menstruate. It should be added that repressed masturbation is apparently refuted by those studies like Hallgren's (10) where a significantly higher incidence of masturbation was found among enuretics. Ackerson (2), however, believes that this that this type of correlation could be determined by popular preconceptions which enhance awareness and consequently the reporting thereof.

Enuresis has been variously described as a "hereditary stigma" (16), "family tradition" (11), "lack of sphincter morality" (5), or "immaturity of the nervous system" (4). In pediatric, neurologic, and urologic literature there is a wealth of etiologic causes for even the most common enuresis—myelodysplasia, irritations (balanitis, vulvitis, etc.), chronic inflammations (nephritis, pyelitis, etc.), nutritional deficiency, allergy, endocrine disorders and a host of others. Training and parental attitudes have also been connected with the presence of enuresis. Low

intelligence and enuresis has been an accepted duality although excellent bladder control before the age of five is not uncommonly seen in mental defectives.

In medical and psychiatric literature numerous articles have appeared indicating that enuresis is associated with emotional problems of children. The high prevalence of enuresis among children evacuated from the larger English cities during World War II has been frequently quoted as a classic instance to support the close association between enuresis and "emotionality."

On the other hand, recent studies where history of occassional enuresis (after age five) was elicited from adult neurotic vs. control groups (17) and regular enuresis (after age five) from neurotic vs. psychotic vs. control groups (18) seemed to imply that enuresis could not be looked upon as an item which might discriminate for future neurotics or psychotics (Table 5).

There seems to be enough lack of corroboration to justify the requestioning of the traditional contention that enuresis is an emotional symptom. The fact is that several studies, including the present, actually contradict such a contention. It appears that enuresis is but an ubiquitous happenstance, the frequency of its appearance being more related to age cut-off point and other statistical mechanics than to adjustment, other emotional symptoms, or future prospects of mental ill-health.

Michaels (15) has made a definite case for enuresis and deliquent psychopathy but he has made clear that he means *persistent enuresis* after age *ten*. Even this is questioned by Ackerson's correlation of enuresis with Juvenile arrests, being .07 and −.25 for boys and girls respectively (above .20 is statistically significant). Nevertheless, there does not seem to be clear justification for considering enuresis as early as the third grade to be a symptom of emotional disturbance. The traditionally accepted duality of enuresis and emotional conflict must now accept a greater burden of proof if it is to maintain its integrity. There is, of course, no insinuation that enuresis cannot still be an emotional symptom, but to qualify it as such would seem to require more sophisticated standards than merely its presence after a certain age, especially if that age is below eight or nine years.

TABLE 5
Summary of Three Studies

	Tapia *et al.*		Winokur *et al.*			Michaels
	N	% Enuretic history*	N	% Enuretic history	Mean age cessation	% Enuretic history
Control	24/82	0.29	15/100	0.15	10.8	24.7
Neurotic	31/87	0.36	9/50	0.18	11.1	16.3
Psychotic	—	—	7/50	0.14	9.7	17.9

* Includes occasional enuresis.

REFERENCES

1. Ackerson, L. Children's behavior problems. II: Relative importance and inter-relation among traits. Behavior Research Fund Monograph. Univ. of Chicago Press, Chicago, 1942.
2. Ackerson, L. and Highlander, M. The relation of enuresis to intelligence, conduct and personality problems, and other factors. Psychol. Clinic, **17:** 119–127, 1928.
3. Anderson, F. N. The psychiatric aspects of enuresis. Am. J. Dis. Child., **40:** 591 & 818, 1930.
4. Brazier, M. A. B. Electroencephalography. Progress in Neurol. & Psychiat., **6:** 227–241, 1951.
5. Ferenczi, S. Psychoanalysis of sexual habits. Internat. J. Psycho-Analysis, **6:** 372–404, 1925.
6. Gerard, M. W. Enuresis: A study in etiology. Am. J. Orthopsychiat., **9:** 48–58, 1939.
7. Gildea, M. C.-L. Community mental health research: Findings after three years. Am. J. Psychiat., **114:** 970–976, 1958.
8. Glidewell, J. C. Mensh, I. N. and Gildea, M. C.-L. Behavior symptoms in children and degree of sickness. Am. J. Psychiat., **114:** 47–53, 1957.
9. Hallgren, B. Enuresis. I. A study with reference to the morbidity risk and symptomatology. Acta psychiat. et neurol. scandinav., **31:** 379–403, 1956.
10. Hallgren, B. Enuresis: A clinical and genetic study. Acta psychiat. et neurol. scandinav., **32:** Suppl. 114, 1957.
11. Healy, W. and Bronner, A. F. *New Light on*

Delinquency and Its Treatment. Yale Univ. Press, New Haven, 1936.

12. KANNER, L. *Child Psychiatry*. 2nd ed. C. C Thomas, Springfield, Ill., 1955.
13. LEVIN, A. Enuresis in the Navy. Am. J. Psychiat., **100:** 320, 1943.
14. MENSH, I. N., KANTOR, M. B. AND DOMKE, H. R. Children's behavior symptoms and their relationships to emotional adjustment, sex and social class. Paper read at the 66th Annual Meeting of the Am. Psychol. A., Washington, D. C., Aug., 1958.
15. MICHAELS, J. J. *Disorders of Character*. C. C Thomas, Springfield, Ill., 1955.
16. MICHAELS, J. J. AND GOODMAN, S. E. Left-handedness. Intercorrelations with enuresis and other related factors in so-called normal children. Arch. Neurol. & Psychiat., 34: 758–763, 1935.
17. PFISTER, H. Enuresis nocturna und Aeuliche Stoerengen in neuropathologischer Bewertung. Monatsschr. Neurol., **15:** 113–147, 1904.
18. TAPIA, F., WERBOFF, J. AND WINOKUR, G. Recall of some phenomena of sleep. J. Nerv. & Ment. Dis., **127:** 119–123, 1958.
19. ULLMAN, C. A. Identification of maladjusted school children. Pub. Health Monogr., No. 7, 1952.
20. WINOKUR, G., GUZE, S. B. AND PFEIFFER, E. Developmental and sexual factors in women: A comparison between control, neurotic and psychotic groups. Paper presented Am. Psychiat. A., Annual Meeting, 1958.

THE PSYCHIATRIC PHYSICIAN AND THE PHENOTHIAZINE TRANQUILIZERS[1]

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That the attitudes of physicians prescribing tranquilizing drugs directly or indirectly affect the evaluation process has been claimed by two comparatively early investigators of this problem (1, 5). One of the implications from these studies is that therapists' attitudes must be controlled in tranquilizer evaluation research. At the present time the Research Department at Spring Grove State Hospital is conducting a double-blind study of the comparative effectiveness of the phenothiazines (Trilafon, Compazine, Vesprin, Thorazine, Sparine and Pacatal) in the treatment of disturbed patients on an admission service of a state psychiatric hospital. Since it is desirable to control the action of all variables that might possibly contribute to error variance in the assessment of treatment results, we have decided to investigate further the subject of attitudes and treatment. For experimental control purposes, we have asked ourselves the following questions: 1) Is there a functional relationship between a physician's attitude toward phenothiazine tranquilizers and his use of these drugs (in terms of recommended dosage schedules)? 2) How is a given physician's attitude related to and influenced by the amount of information he has regarding phenothiazine tranquilizers? Is information functionally related to use? And, finally, since a certain amount of data concerning treatment success is already available from our comparative study, we are in a position to make a preliminary investigation into a third, more specific question: 3) To what extent is the attitude variable operative in an experimental design utilizing the double-blind technique?

[1] This investigation was conducted at Spring Grove State Hospital and supported in part by Research Grant No. MY-2152 from the National Advisory Mental Health Council, National Institute of Health, U.S. Public Health Service and administered by Friends of Psychiatric Research, Inc., Baltimore, Maryland.

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METHOD

Three inventories concerning (a) attitudes toward phenothiazine tranquilizers, (b) information regarding dose, indication for use and side effects of phenothiazine tranquilizers, and (c) the physician's use of these drugs in varying situations, were presented to 34 resident and staff physicians at the Spring Grove and Springfield State Hospitals in Maryland. All of the physicians completed the attitude and information inventories, whereas only 30 completed the one on use.

Attitudes toward phenothiazine tranquilizers were ascertained through a 24-item inventory developed by Mason and Sacks (4). These 24 items were initially selected from 64 statements culled from interview data and references to the literature. Each item was judged by four psychiatrists and eleven clinical psychologists as to its bearing on physicians' confidence in drug therapy. The 24 items finally selected were consistently classified by the judges as being either favorable or antagonistic to drug therapy. Initial validation results showed the scale correlated significantly with the percentage of patients each physician placed on tranquilizing medication. In this present study the items were made specific for the phenothiazines and the scoring modified according to the following schema: Each physician re-

sponding to the inventory stated his degree of agreement with each item through the use of a 5-point rating scale. A highly favorable attitude toward phenothiazine tranquilizers indicated by an inventory item received a score of 1; a noncommittal attitude received a score of 3; a most negative attitude was scored 5. Thus, for all 24 items of the inventory, a score of 24 would reflect the most favorable attitude possible. A score of 120 would be obtained if all 24 items were responded to in the most negative fashion.

Physicians' information regarding phenothiazine tranquilizers was measured by a 20-item true-false questionnaire tapping knowledge of use, side effects, and target

TABLE 1

Questionnaire Sampling Information About Phenothiazine Tranquilizers

The following 20 items are "true-false" items. Try to answer all items as true or false even though you may have qualifying beliefs connected with your answers.

1. It is advisable, for highly disturbed patients, to step up the dosage of phenothiazine tranquilizing drugs at 1 or 2 day intervals, if no or little positive response has been obtained.	true	false
2. Patients hospitalized with mild depression and loss of interest, and who have a good secondary gain from hospitalization, are good candidates for phenothiazine tranquilizers.	true	false
3. If a patient on phenothiazine tranquilizers has developed Parkinsonism, the time and drug spent on that treatment has been wasted.	true	false
4. Phenothiazine tranquilizers tend to attack bothersome ideation when this is associated with subjectively felt discomfort.	true	false
5. Development of Parkinsonism upon administration of phenothiazine tranquilizing drugs is highly undesirable from the point of view of delaying psychiatric improvement.	true	false
6. Patients with delusional ideation, who at the same time do not show a considerable degree of discomfort, cannot be appreciably helped with phenothiazine tranquilizers.	true	false
7. The target symptoms of phenothiazine tranquilizing drugs are delusions and hallucinations.	true	false
8. Phenothiazine tranquilizer-induced Parkinsonism does not always indicate a reduction of the tranquilizing medication, but can be treated with cogentin, artane or other drugs.	true	false
9. All phenothiazine tranquilizers have essentially the same sedative effect.	true	false
10. Hostility, destructiveness, etc., in a psychotic individual can be alleviated (as concerns this destructiveness) if the patient's "specific" phenothiazine tranquilizer is found.	true	false
11. An acting out psychopath without notable self-criticism is a fair condidate for phenothiazine tranquilizing medication.	true	false
12. In a psychiatric hospital setting, the recommended initial dose of compazine is 10 mg TID and that of thorazine 50 mg TID.	true	false
13. Immobilization and withdrawal with underlying strong but concealed anxiety cannot be helped by a tranquilizing drug.	true	false
14. Tranquilizer-induced jaundice is connected with a serious form of hepatitis and an extensive, permanent liver damage.	true	false
15. A very disturbed patient many times will show a much better response to a given tranquilizer if the drug is stepped up at frequent intervals.	true	false
16. Once a patient has developed Parkinsonism on a given tranquilizing drug, the patient should not be given the same drug again.	true	false
17. The appearance of agranulocytosis depends mainly on the size of the dose of a tranquilizer.	true	false
18. Without considering other factors, the more disturbed a patient is, the higher a dose of tranquilizer can be tolerated without drowsiness.	true	false
19. Most practitioners agree that tranquilizing drugs alleviate subjective "discomfort."	true	false
20. Hostility, not associated with guilt and anxiety, can most likely be helped by phenothiazine tranquilizing drugs.	true	false

symptoms. The items of this questionnaire were chosen from a list of representative items suggested by three supervising psychiatrists. To avoid ambiguity only those items were selected on which there was agreement as to the clarity of the item and correctness of the answer. Table 1 presents this questionnaire in its entirety.

Physicians' "use" of the phenothiazine tranquilizing drugs was inferred from response to a 25-item questionnaire containing several hypothetical clinical situations. This questionnaire also contained an item asking physicians to rate their own use of drugs relative to other physicians, as marked, average, or minimal. An example of the clinical situation items is the following:

Assume you are on an admission service and are responsible for a 45 year old, physically healthy, female patient. This is her first admission. She seems to suffer from an agitated depression. She is restless, preoccupied with obsessive ruminations, hyperirritable, and markedly anxious. Delusional or otherwise psychotic thinking is not present. You have decided to treat this patient with prochlorperazine (Compazine).

a. *What initial dose would you use?*
b. *Should no effects be immediately observable, how long would you wait before stepping up the dose?*
c. *What would you consider to be a safe maximum daily dose?*
d. *Should the patient persist in showing no change in symptomatology, how long would you continue to treat this patient with phenothiazine tranquilizers (before you administer a different therapeutic regime)?*
e. *What is the percentage of this type of patient in your experience which has required phenothiazine tranquilizers?*

In the construction of this questionnaire it was assumed that physicians who tend to use drugs more aggressively would prescribe larger initial doses, step up the dose more readily, and use higher maximum doses, etc. The response for each physician for any one item was scored 1, 2 or 3 depending on whether the response reflected a minimal, moderate or marked use of the drug in relation to the overall responses of the group. These responses were then summed for the 25 items and averaged to yield a total score ranging from 1 to 3.

Although the measurement of drug usage via a questionnaire is valid only on an *a priori* basis, this technique has an advantage over the actual use of drugs as ascertained from clinical records. Very few physicians are on the same or similar wards in a given hospital. This implies that although physicians treat the same diagnostic categories of patients, the symptomatic manifestations vary considerably. In order to have comparable data (for a sample of physicians large enough to warrant statistical treatment), it was necessary to resort to a questionnaire which presented *identical* clinical problems to all physicians.

RESULTS

Resulting attitude scores for the 34 physicians involved in the study ranged from 40–87. Twelve, or approximately one-third of the group whose scores ranged from 40–53 were designated the favorable attitude group, while eleven whose scores ranged from 60–87 were designated the unfavorable attitude group. Data on the drug usage inventory were available for all the physicians in the favorable attitude group and for all but one in the unfavorable attitude group. The difference in the respective mean usage scores of 2.00 and 2.11 for these groups was not significant ($t = 1.00$, 21 df, $p > .10$); nor was the correlation of .03 between attitude and drug usage significant. There is consequently no indication that for our population, attitudes toward phenothiazine tranquilizers are functionally related to the inventoried use of these drugs.

Attitudes are, however, significantly related to self estimates of drug usage. (Interestingly enough, these estimates were found to be unrelated to comparative drug usage as

determined by the inventory.) Of the 28 physicians who completed the self rating scale on drug usage, seven rated themselves as "minimal users" and seven as "marked users," with the rest falling in the intermediate or noncommittal range. The mean attitude score for the minimal users was found to be 67.9, which is in the unfavorable direction, while that for the marked users was 53.9. It therefore seems indicated that physicians with relatively negative attitudes toward phenothiazine tranquilizers, compared with physicians with positive attitudes, think of themselves as using drugs less aggressively ($t = 4.44$, 12 df, $p < .001$). As seen above, the two groups could not be significantly differentiated in terms of drug usage inventory scores, which leads one to suspect that physicians' actual therapeutic practices as concerns phenothiazine tranquilizers are very likely not related to their attitudes, even though they believe them to be so related.

It might be expected that there would be a positive, straight-line relationship between physicians' attitudes toward phenothiazine drugs and the amount of information they have amassed regarding them. However, this type of relationship was not found in the analysis of data from this study. If anything, the distribution of the data suggested a curvilinear relationship, since the extreme attitude groups, favorable and unfavorable, responded incorrectly to 11.6 per cent and 12.9 per cent of the information scale items, respectively, and the intermediate attitude group was wrong on 16.8 per cent of the items. This result probably reflects a chance distribution ($eta = .247$, $p > .10$), but is in accord with the psychological research finding that extremely negative attitudes toward a given topic are associated with heightened perceptual sensitivity toward that topic (2).

When the physicians' information levels are compared to their use of drugs, a significant relationship emerges. Those physicians with a greater amount of information tend significantly to use drugs more aggressively in hypothetical situations. The product-moment correlation coefficient of .41 obtained between information and use indicates a certain amount of covariation between these two measures. Data illustrative of this is the finding that those physicians who were wrong on 10 per cent or less of the information items obtained an average rating of 2.2 on the 25-item drug usage inventory, while those who were wrong on 20 per cent or more of the information items averaged a usage score of only 1.91. As previously noted the smaller the usage score, the less aggressively a physician tends to use drugs (relative to the other physicians studied) in the sample clinical situation presented to him.

In support of the findings already reported the following results relative to our third question on attitudes and double-blind methodology also bear consideration. Of the 34 physicians on whom the relationships among attitudes, information and usage were determined, eight had been directly involved in the comparative drug research project which originally prompted this investigation. These physicians had been responsible for the treatment of 101 patients, to whom they had administered phenothiazine drugs in a double-blind fashion for two to six weeks depending upon responsiveness of the patient. Except for a required minimum dosage, the eight physicians were at complete liberty to manipulate dosage in terms of the number of capsules administered per day. It was therefore possible to measure the physicians' actual use of drugs in similar situations in terms of average daily dosage, highest daily dosage, the number of times the dosage was increased and a combined measure of all three indices. Actual therapeutic results were also available in terms of the Multidimensional Scale for Rating Psychiatric Patients (MSRPP) (3) and global psychiatric evaluations which were completed by an independent team of investigators who were also unaware of the specific treatment involved in each case.

While the number of physicians studied

in this clinical-research setting was only eight, and therefore not amenable to statistical inference, the results nevertheless are of interest. When these physicians (all of whom had differing attitudes) were compared on all indices of actual drug usage, it was found that their therapeutic practices did not vary as a function of their attitudes toward phenothiazine tranquilizers ($F < 1$).

But how did the differential attitudes of the physicians affect the outcome of their treatments? In an attempt to answer this question, the patients of the eight physicians were then compared as to changes in severity of illness (using both MSRPP and global psychiatric evaluation). In this comparison, the patients' initial degrees of illness were controlled statistically via the analysis of covariance, with the resulting finding that the patients of each of the eight doctors did not improve to a differential degree (F cov. < 1). The eight physicians not only used phenothiazine tranquilizers in a similar fashion, but also obtained a notably similar degree of improvement from their patients. Of course, it must be iterated that the physicians did not know which of the six phenothiazine tranquilizers (plus active and inert placebos) they were administering. This finding supports the conclusion that the use and effectiveness of the phenothiazine tranquilizers studied here is distinct from whatever attitudes the physicians have concerning these drugs. It would consequently appear that experimental control of the attitude variable in double-blind studies concerned with the effectiveness of phenothiazine treatment is not as essential as indicated by past research.

SUMMARY

An attitude scale and an information inventory concerning phenothiazine tranquilizers were administered to thirty-four resident and staff psychiatrists from two state psychiatric hospitals. Thirty of these physicians also completed a questionnaire concerning use of phenothiazine tranquilizers in hypothetical clinical situations. Results obtained suggest that: 1) there is no relationship between physicians' attitudes toward phenothiazine tranquilizers and their use of these drugs; 2) physicians with a greater degree of information use phenothiazine tranquilizers in a more aggressive fashion than those possessing less information about phenothiazine tranquilizers; 3) a greater degree of information regarding phenothiazine tranquilizers might possibly be associated with extreme positive and negative attitudes toward phenothiazine tranquilizers; 4) physicians' ratings of their own use of drugs do not seem related to actual use, but rather to their attitudes. Actual use appears to be independent of attitudes and physicians' opinions regarding their practice.

In addition, data were available for eight physicians who treated a total of 101 patients as part of a double-blind comparative study of six phenothiazine tranquilizers. In analyzing these data, it was found that physicians' attitudes toward phenothiazine tranquilizers did not affect their actual use of them. Further, changes in patients' severity of mental illness did not seem to be a correlate of physicians' attitudes.

REFERENCES

1. Feldman, P. E. The personal element in psychiatric research. Am. J. Psychiat., **113:** 52–54, 1956.
2. Lindzey, G. and Rogalsky, S. Prejudice and identification of minority group membership. J. Abnorm. & Social Psychol., **45:** 37–53, 1950.
3. Lorr, M. *The Multidimensional Scale for Rating Psychiatric Patients: Hospital Form I.* V. A. Tech. Bull., TB 19-507, Washington, D. C., 1953.
4. Mason, A. S. and Sacks, J. M. Measurement of attitude toward the tranquilizing drugs. In Tr. 2nd Res. Conf. Chemotherapy in Psychiatry, **2:** 118–122, 1958. V. A., Office of the Medical Director, Washington, D. C.
5. Shabshin, M. and Ramat, J. Pharmacotherapeutic evaluation and the psychiatric setting. A. M. A. Arch. Neurol. & Psychiat., **75:** 362–370, 1956.

PATIENTS SCREENED AND CRITERIA USED FOR SELECTING PSYCHOTHERAPY CASES IN A MENTAL HYGIENE CLINIC

M. A. BAILEY, PH.D.,[1] L. WARSHAW, PH.D. AND R. M. EICHLER, PH.D.

In 1953, Eichler (1) surveyed the population of patients in psychotherapy at the New York Regional Office of the Veterans Administration and found that population to vary significantly from the veteran population of the New York City area in terms of race, religious background, and sex. In addition to studying the relationship of the patient sample and census data, Eichler (1, 2) surveyed the psychotherapy patient population with respect to items of clinical information which could not be compared with population statistics. Other investigators (3, 4, 5) have reported a significant relationship between utilization of psychotherapy and factors such as religious background, race, and other socio-cultural phenomena. The previous investigation by Eichler dealt with patients already in psychotherapy. Eichler did not study the characteristics of patients applying for treatment or the selective factors involved in assigning patients to various types of therapies.

The purpose of the present study was to determine whether the patients applying for treatment at the New York Regional Office were representative of the greater New York City veteran population, and to discover whether patients selected for psychotherapy differed significantly from those not selected. The investigators hypothesized that: 1) The patients screened in this clinic will be generally representative of the veteran population in those areas in and around New York City served by this office.[2] 2) Assignment by screening psychiatrists is largely determined by demographic and clinical characteristics related to high socio-economic status, high education, intrapsychic complaints, expressed desire for psychotherapy, and psychoneurotic diagnoses.

[1] Veterans Administration Regional Office, 252 Seventh Avenue, New York City.

METHOD

In order to investigate the nature of the patient population applying for outpatient treatment, and the relationship between assignment and certain normative data, in the Mental Hygiene Treatment Group, Psychiatry and Neurology Unit of the New York Regional Office, a personal data card was completed on every patient tested by a psychologist as a part of the screening process during the period of May 1956 to January 1957. The total number of cases considered was 549. The subjects consisted of 539 males and 10 females. The items of information obtained were: age, education, occupation, religious background, race, sex, nature of complaint, treatment requested by the patient, treatment recommended by psychologists following psychodiagnostic examination, and diagnoses by testing psychologists and therapists. Assignment of patients to treatment was made by a screening psychiatrist. In those areas which could be compared with census data, chi-squares were computed. In those areas where comparisons with population statistics were not possible, the data were tabulated and later utilized to obtain comparisons between various treatment groups in order to study criteria for assignment to various treatment activities and their relationship to prognosis. Prognosis will be dealt with in a subsequent paper. In testing the significance of the relationships between normative and/or clinical data to assignment, only those patients assigned to

[2] The New York Regional Office services veterans in Manhattan, Bronx, Queens, Staten Island, and in Nassau, Suffolk, Westchester, Putnam and Orange Counties.

TABLE 1

Age Distribution Table of Patients Screened in a Mental Hygiene Clinic

Age	Psycho-therapy	Psycho-somatic	Insulin	Neur-ology	Unas-signed	Total
18–22	8	4	0	2	2	16
23–27	45	26	3	5	7	86
28–32	38	38	3	4	11	94
33–37	63	75	3	5	16	162
38–42	32	45	3	2	10	92
43–47	16	36	2	2	8	64
48–52	8	12			2	22
53–57		3			2	5
58–62		4				4
63–67	1	2				3
68		1				1
Totals	211	246	14	20	58	549

the psychotherapeutic and psychosomatic[3] forms of treatment were included. This comprised 83.2 per cent of all the patients.

RESULTS

PATIENTS APPLYING FOR TREATMENT

A summary of the findings may be seen in tables one through six.

Age: The age of the present sample ranged from 18 to 64 years. The mean for the total population was 35.36 with a standard deviation of 7.32. This patient population was composed primarily of WWII and Korean veterans. At the time these data were collected, the combined average age for WWII and Korean veterans as compiled by the New York Regional Office for veterans in the New York City area was 35.37 (7). Inspection revealed no remarkable difference between the average age of the patient population and the combined average age of WWII and Korean veterans. Refer to Table 1.

Education: The range of education for the present sample was from three to twenty years of schooling. The mean number of years of schooling for the total patient population was 11.42 with a standard deviation of 2.59. A comparison of this patient population with the veteran population at large (6) revealed no significant difference in the number of years of schooling when tested by chi-square. Refer to Table 2.

[3] Psychosomatic treatment refers to treatment by tranquilizers and sedatives only.

TABLE 2

Composite Table of Demographic and Clinical Data on Patients Screened in a Mental Hygiene Clinic

	N	Patients	
		Per Cent	Census Data
Amount of Schooling*			
Elementary	93	16.9	22.9
Some High School	179	32.6	20.8
High School Graduate	133	24.2	31.6
Some College	82	14.9	11.2
College Graduate	62	11.2	12.4
Occupations*			
Professional-Technical	41	10.1	11.7
Business, Managerial	17	4.2	15.8
Clerical	98	24.2	8.1
Semi-Technical	121	29.9	44.5
Sales	59	14.6	6.5
Laborers and Services	69	17.0	12.5
Unemployed	144	(26.2)	(9)
Religious Background†			
Catholic	237	43.1	45
Protestant	133	24.2	25
Jewish	134	24.9	25
Other	45	8.2	5
Race†			
Negro	65	11.8	11
White	484	88.1	89
Sex*			
Male	539	98.1	98.5
Female	10	1.8	1.5
Nature of Complaint			
Intra-Psychic	259	47.2	
Somatic	225	40.9	
Other	63	11.5	
None	2	.3	
Treatment Requested by Patient			
Medication	191	34.8	
Psychotherapy	211	38.4	
Do Not Know	124	22.6	
Misc.	23	4.2	
Previous Treatment			
Psychotherapy	232	42.2	
No Psychotherapy	317	57.5	
No Previous Treatment	(271)		
EST and/or IST	(31)		
Medication	(13)		
Do Not Know	(2)		

* Census data based upon United States veterans.

† Census data based upon non-veterans in the area served by the New York Regional Office.

TABLE 3

Tabulation of Agreement Between Diagnosis by Therapists and by Psychologists Following Psychological Tests

	Psychotic	Psychoneurotic	Neurological	Total
Psychotic	209	42	19	270
Psychoneurotic	24	224	20	268
Neurological	0	2	9	11
Total	233	268	48	549

Religious Background: The percentages of patients of different religious backgrounds did not differ significantly from those reported for the general population in the area of New York City served by this clinic (2). Refer to Table 2.

Race: The percentage of Negroes in this sample was not remarkably different from the 11 per cent reported for the New York City area served by this clinic (1). An exceedingly small percentage (included in the 88.2 per cent Whites) were of other races. Refer to Table 2.

Sex: At the peak of mobilization, the percentage of women in the armed forces was 1.54 (Encyclopedias Britannica and Americana). No remarkable difference was observed between the percentage of women in the armed forces and the percentage of female veterans applying for treatment in this clinic. Refer to Table 2.

Occupation: A comparison of the patient population with the veterans population at large for occupations (6) yielded a chi-square of 21.54, significant beyond the .01 level. Occupational data for New York City veterans were not available. The comparison revealed that although both populations were similar for the professional, labor, and service categories, the patient population had a considerably smaller per centage in the managerial and semi-technical categories and a considerably higher percentage in the clerical and sales categories than were reported for the veteran population at large (6). No data were available on unemployment in the veteran population. However, the 26.2 per cent unemployed in our sample is far greater than the nine per cent unemployed in the general population in this area. Refer to Table 2.

Diagnoses by Testing Psychologists and Therapists: When the diagnoses, made by psychologists as a product of psychodiagnostic testing, were matched with those rendered by the therapists, a highly significant correspondence of diagnoses was observed. A chi-square of 368.41 was obtained which was significant far beyond the .01 level. Psychological test data were available to all the therapists prior to the initiation of psychotherapy. Refer to Table 3.

PATIENTS ASSIGNED TO TREATMENT

Of the 549 patients surveyed, 211 (38.4 per cent) were assigned to psychotherapy, 246 (44.8 per cent) were assigned to treatment in the psychosomatic clinic, 20 (3.6 per cent) were assigned to the neurology service (from psychiatric screening), 14 (2.6 per cent) were assigned to insulin subcoma therapy (from psychiatric screening) and 58 (10.6 per cent) remained unassigned for a number of reasons, such as change of residence, ineligibility, etc. Data for patients assigned to treatment in the psycho-

TABLE 4

Diagnosis, Treatment Recommended by Psychologists and Assignment to Treatment

	Assigned to Psychotherapy	Assigned to Psychosomatic	Total
Psychotics Recommended for:			
Psychotherapy	78	55	133
Psychosomatic	3	37	40
Other	12	33	45
Total	93	125	218
Non-Psychotics Recommended for:			
Psychotherapy	101	50	151
Psychosomatic	8	32	40
Other	9	39	48
Total	118	121	239

somatic clinic and psychotherapy may be seen in Tables 4, 5 and 6.

Age: The mean age of patients assigned to psychotherapy was 33.61 with a standard deviation of 7.5, and the mean age for patients assigned to psychosomatic treatment was 37.30 with a standard deviation of 7.7. The patients assigned to psychotherapy were younger than the patients assigned to psychosomatic treatment. The difference in ages was significant beyond the .01 level ($t = 5.25$). Refer to Table 1.

Education: The mean number of years of schooling for patients assigned to psychotherapy was 12.5 with a standard deviation of 3. The mean number of years of schooling for patients assigned to psychosomatic therapy was 10.6 with a standard deviation of 2.4. Patients assigned to psychotherapy had more years of schooling than patients assigned to psychosomatic therapy. The difference in number of years of schooling was significant beyond the .01 level ($t = 7.91$). Refer to Table 5.

TABLE 5

Composite Table of Demographic and Clinical Data on Patients in Psychotherapy (PT) and Psychosomatic (PS) Treatment

	PT	PS		PT	PS
Schooling			Race		
Elementary	21	59	Negro	14	38
Some High School	49	93	White	196	208
H. S. Graduates	54	57	Sex		
Some College	45	25	Female	4	4
College Graduates Or More	42	13	Male	207	242
Occupations			Diagnosis By Therapists		
Professional	17	7	Psychotic	85	115
Technical	10	2	Non-Psychotic	126	131
Business, Managerial	10	3	Nature of Complaint		
Clerical	38	42	Intra-Psychic	130	86
Semi-Technical	64	56	Somatic	47	133
Sales	19	18	Others	34	25
Labor and Services	12	45	None	0	2
Unemployed	41	73	Treatment Requested		
Religious Background			Medication	29	126
Catholic	79	112	Psychotherapy	139	50
Protestant	51	61	Do Not Know	39	58
Jewish	65	56	Misc.	4	12
Other	16	17	Previous Treatment		
			Psychotherapy	118	89
			Other or None	92	157
			Do Not Know	1	
N	211	246			

TABLE 6

Amount of Schooling for Negro and White Patients Applying for Treatment

	Negro	White
Elementary	18	75
Some High School	19	160
High School Graduate	13	120
Some College	12	70
College Graduate or More	3	59
Total	65	484

Occupation: Patients in higher-level occupations tended to be assigned to psychotherapy while patients in lower-level occupations were likely to be assigned to the psychosomatic clinic. The relationship between assignment and occupational level was significant beyond the .01 level (chi-square = 39.38). Refer to Table 5.

Religious Background: There was no relationship between assignment and religious background. Refer to Table 5.

Race: Negro patients tended to be assigned to treatment in the Psychosomatic clinic to a greater extent than White patients. However, inasmuch as Negro patients tended to have fewer years of schooling than the White patients, the difference in assignment may be partly related to the educational factor. The difference in amount of schooling between Negroes and Whites closely approached significance (chi-square = 9.48, $p = .06$). Refer to Table 6. The chi-square between assignment and race was significant beyond the .01 level (chi-square = 8.21). Refer to Table 5.

Diagnoses: There was no relationship between diagnoses made by psychologists on the basis of psychological tests and assignment, or between diagnoses made by therapists and assignment. Neither was

there significant relationship between the diagnoses made by psychologists as a result of psychodiagnostic testing and the treatment recommended by psychologists. Refer to Tables 4 and 5.

Nature of Complaint: Patients with intrapsychic complaints were likely to be assigned to psychotherapy while patients with somatic complaints were likely to be assigned to treatment in the psychosomatic clinic. This relationship was significant beyond the .01 level (chi-square = 42.29). Refer to Table 5.

Treatment Requested: Those patients who requested medication were assigned predominantly to treatment in the psychosomatic clinic while those patients who requested psychotherapy were more frequently assigned to psychotherapy. This was significant far beyond the .01 level (chi-square = 104.31). Refer to Table 5.

Treatment Recommended by Psychologists: Approximately 60 per cent of the patients tested were recommended for psychotherapy by the psychologists and 54 per cent of this number were assigned to psychotherapy. Psychologists recommended 17.8 per cent of the patients tested for psychosomatic treatment. Of these, 70 per cent were actually assigned to psychosomatic treatment. The chi-square of 87 was significant beyond the .01 level. Refer to Table 4.

Previous Treatment: Information in this area was available for 548 cases. Forty-two per cent of the cases had received psychotherapy in the past. Approximately 50 per cent of those who had had psychotherapy were assigned to psychotherapy while 29 per cent of those who had had no previous psychotherapy were assigned to this form of treatment. A chi-square of 24.09 was significant beyond the .01 level. Refer to Table 5.

DISCUSSION

It was hypothesized that veterans who apply for treatment at the Psychiatry and Neurology Unit of the New York Regional Office would be representative in certain aspects of the veteran population served by this office. This hypothesis was substantiated in most aspects of the demographic data surveyed. Consequently, it is inferred that the presence of emotional disturbance is not related to demographic population characteristics. However, the high ratio of unemployment in the patient population and differences in employment categories indicate—as would be expected—a relationship between emotional disturbance and impaired vocational adjustment. Inasmuch as it was not always possible to obtain data on the non-patient veteran population in the New York City area, national veteran population data were used for comparisons in amount of schooling, occupations, and sex. Also, the non-veteran population in the area served by this office was used for comparisons in religious background and race. Findings resulting from such comparisons are offered tentatively inasmuch as these findings rest on the assumption that the New York City veteran population is similar to the national veteran population or the non-veteran New York City population in these instances.

An evaluation of the patient's complaints and the types of assistance requested by the patients revealed that more than one half of this population seemed to be unaware of the fact that their difficulties had an emotional basis.

The results of this study confirmed the hypothesis that assignment to psychotherapy is closely related to higher educational and occupational levels, intrapsychic rather than somatic complaints, expressed desire for psychotherapy, psychologists' test recommendations, and previous experience in psychotherapy. In addition to these criteria, age is a factor in assignment, younger patients being more readily assigned to psychotherapy than older ones. The diagnosis appears to play an insignificant role in assignment, as those making assignments do not consider diagnosis a valid prognostic

indicator. In addition, the diagnosis does not take into consideration a number of factors which are closely related to assignment for psychotherapy. While race was related to assignment in that Negroes tended to be assigned to psychosomatic rather than psychotherapeutic treatment, this appeared to be in part a function of education. Of the three findings in Eichler's survey (race, religious background, and sex), only race was found to be related to assignment to psychotherapy. None of the three factors seemed related to applying for treatment. However, Eichler's survey at this clinic dealt with patients already in psychotherapy and therefore his survey cannot be directly compared to the present study.

SUMMARY AND CONCLUSION

Five hundred and forty-nine patients screened and assigned for treatment at the Psychiatry and Neurology Unit of the New York Regional Office were surveyed for normative data. The demographic characteristics of this patient population were compared with veterans in the area served by this office. The relationship between demographic characteristics and assignment was also investigated. The patient population was found to be generally representative of the veteran population served by this office. The patients differed significantly from the veteran population at large in vocational achievement in that the patients were less successful and had a greater incidence of unemployment. Diagnostic information revealed that the patient population was about equally divided between psychoneurotic and psychotic diagnoses. Approximately 50 per cent of the patients had complaints and interests which did not indicate a desire for psychotherapy. Assignment to psychotherapy is related to high educational and occupational level, relative youth, intrapsychic rather than somatic complaints, expressed interest in psychotherapy, psychologists' test recommendations, and previous experience in psychotherapy. The relationship between race and assignment seemed to be partly due to education. Such factors as religious background and diagnosis failed to reveal a significant relationship to assignment.

REFERENCES

1. Eichler, R. M. A survey of patients in individual psychotherapy. Unpublished manuscript. 1953. Available at: Library, Veterans Administration, New York Regional Office, New York.
2. Eichler, R. M. and Lirtzman, S. Religious background of patients in a mental hygiene setting. J. Nerv. & Ment. Dis., **124:** 514–517, 1956.
3. Hollingshead, A. B. and Redlich, F. C. *Social Class and Mental Illness.* Wiley, New York, 1958.
4. Roach, J. L., Gurrslin, O. and Hunt, R. G. Some social-psychological characteristics of a child guidance clinic caseload. J. Consult. Psychol., **22:** 183–190, 1958.
5. Scott, W. A. Social psychological correlates of mental illness and mental health. Psychol. Bull., **55:** 65–87, 1958.
6. U. S. President's Commission on Veterans' Pensions. *Veterans in Our Society. Data on the Conditions of Military Service and on the Status of the Veteran.* Government Printing Office, Washington, 1956.
7. U. S. Veterans Administration, New York Regional Office, Information Service. *News Release.* 1958.

THE PSYCHIATRIC CONSULTATION IN POSTGRADUATE MEDICAL TEACHING

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The post-graduate or residency training is the critical period in which the values and technical competence of the future clinician are crystallized into a sense of professional identity. It is at this time that learning acquired in the undergraduate programs of psychiatric teaching is either consolidated into clinical work or largely discarded as extraneous and irrelevant.

In 1946, a medical-psychiatric liaison service was established at The Johns Hopkins Hospital and School of Medicine with the primary goal of teaching residents and medical students of the medical service a better understanding of the role of personality functions in the genesis and evolution of patterns of disease. Lidz and Fleck have reported on the qualitative functioning of this service (4). The present report summarizes an effort at more comprehensive evaluation of the effectiveness of such teaching efforts at the post-graduate, or resident level.

SOURCES OF THE DATA

The data are derived from two sources. The first is an intensive study of 60 consecutive requests for psychiatric consultation in 1954–55. The purpose of this study was the investigation of the psychiatrist's participation in interpersonal patterns of disturbed behavior of patients on a medical ward. It provided opportunity for intensive observation of medical house staff in relation to disturbed patients. Other aspects of this study will be reported elsewhere (6). This intensive study has been supplemented, for purposes of this report, by data from the annual statistics of the Psychiatric Liaison Service and the Statistics Department of The Johns Hopkins Hospital.

The traditions and organization of responsibility within the Osler Medical Service at The Johns Hopkins Hospital are favorable to such a study. The decision to request all consultations rests in the hands of the medical intern and his assistant resident. The liaison psychiatrist, when called upon, acts as advisor and clinical collaborator but ultimate responsibility and authority remain in the hands of the resident medical staff.

For the intensive study, the same psychiatrist (M.M.) answered 60 consecutive requests for psychiatric consultation from medical residents on two medical wards of the Osler Medical Service. The psychiatrist's office was immediately adjacent to one of the medical wards, a fact which encouraged verbal requests for consultation rather than written requests. Twenty-five per cent of the requests for consultation came up in chance meetings with medical staff in the corridors, on the medical wards, or in the dining room. This suggests the value of proximity in the liaison psychiatrist's work.

FINDINGS FROM THE SPECIAL STUDY

During the study period, 678 patients were admitted to the medical wards. The medical interns and assistant residents asked the consulting psychiatrist to see 60 (8.8 per cent) of the total population of the medical wards studied.

A comparison was made of the sample

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of 60 patients the liaison psychiatrist was asked to see, with the total population of the medical wards (678 patients) in respect to age, sex, duration of hospital stay, mortality rate, and financial or income status.[2] With respect to age and financial status, the consultation group were a fair sample of the ward population. The patients selected by the medical residents for psychiatric consultation contained a slightly higher proportion of female patients, of longer-stay patients, and had a lower mortality rate during their hospital stay. Nineteen per cent of the total medical population died during their Osler admission. The people admitted to this service are obviously a sick group of people. In fact, a follow-up of the 60 patients seen by the psychiatrist approximately one year after the consultation revealed that although only two of the group had died during their hospital stay, 15 (25 per cent) of the patients had died by the time of follow-up study. The psychiatrist's patients were obviously also a seriously ill group of people. Analysis of the medical diagnoses revealed that they too suffered from multiple and generally chronic physical conditions.

Fourteen of the 60 patients seen by the psychiatrist required psychiatric hospitalization at the time of the consultation or shortly thereafter. Another fraction, approximately one-sixth of the group, required some definitive psycho-therapeutic effort on an out-patient basis.

Consulting psychiatrists have at times been used as a "last resort" or as an attempted means of hopefully expediting some "disposition" of patients in circumstances where other means seemed unlikely. For this reason, we were interested to note that the requests for psychiatric consultation were clearly not so motivated. Thirty-five per cent of the requests were made during the first third of the patient's hospital stay; 52 per cent during the middle third, and only 13 per cent during the last third of the patient's hospital stay. Detailed study of the requests supports, we believe, what these facts suggest, *i.e.*, that these requests for psychiatric consultation were not merely expressions of an end-point of medical interest and responsibility.

A majority of the patients were seen by the psychiatrist for multiple rather than single interviews. Frequent discussions were held with relatives and particularly with house staff and nurses. In a substantial minority of cases, the psychiatrist's efforts with his patient probably deserved the term "brief psychotherapy." A maximum of 21 interviews was held with one patient. The average for each of the 60 consultations was three interviews with the patient and five discussions between the psychiatrist and the intern or assistant resident.

DISCUSSION

The goal of the study was to provide some answers to the questions implicit in Kaufman's succinct statement, "one of the basic facts of life for the psychiatrist in a general hospital is the simple and pragmatic one as to whether he is of value to other members of the staff" (3).

On a medical service where the house officers bear maximum responsibility for patient care, the liaison psychiatrist was asked to see 8.8 per cent or about one in 11 patients admitted to the medical wards during the period of a special study. This figure derives from a teaching medical service that primarily admits the sicker patient who stays less than 30 days in the great majority of cases. Although the intensive study of these psychiatric consultations came to no special notice from the medical resident staff, there remained the possibility that the consulting psychiatrist's interest in the project could communicate and thereby increase the number

[2] The assistance of Mrs. Eleanor Entorf, now on the Social Work staff of the Sheppard and Enoch Pratt Hospital, Towson, Maryland, is gratefully acknowledged.

TABLE 1

Number and Per Cent of Total Medical Ward Population For Whom Psychiatric Consultation was Requested By Medical House Staff

12 month period (July 1–June 30)	Total patients on ward service	No. consultations requested	Per cent
1955–1956	1972	136	6.9%
1956–1957	1858	91	4.9%
1957–1958	2233	175	7.8%
*1958–1959	1227	104	8.5%
Total:	7290	506	6.9+%

* 6 months, July 1, 1958–Dec. 31, 1958.

of requests for psychiatric consultation. We therefore calculated from the records of the Psychiatric Liaison Service, the annual rates of request for psychiatric consultation in relation to total population of all medical wards for a period of three and one-half years (July 1, 1955–December 31, 1958). Table 1 suports the conclusion that the figure attained in the special study was not greatly different from the rate of request for psychiatric consultation at other times and with other interested and able liaison psychiatrists. We conclude that even on a medical service that primarily admits the more seriously ill patient, adequate staffing by able liaison psychiatrists result in psychiatric referral of about one in 11 or 12 patients admitted to the ward.

The perception of a patient as sufficiently disturbed to warrant calling in a psychiatrist is obviously an elastic and multidetermined decision. Elsewhere, we have suggested that the decision to request psychiatric consultation can only be understood as a function of the physician-patient relationship (5). The decision occurs, in our view, when the patient's behavior induces a high level of uncertainty in the physician and/or nurses in a situation of felt responsibility, *i.e.*, the patient's behavior cannot be dismissed as idiosyncratic or otherwise irrelevant. This uncertainty in the clinician can take a more intellectual form ("legitimate" or diagnostic uncertainty) or a more mediate, affective form. Briefly restated, uncertainty may be felt as puzzlement or subjective distress. The latter tends to threaten the sense of professional identity of the clinician or nurse (1, 2). Either type of uncertainty, however, if sufficiently enduring and without prospect of relief, may result in a request for psychiatric consultation.

Bearing these facts in mind, it is not surprising that there is variation in the individual resident's perception of his patients as disturbed and of himself as a clinician being in need of the psychiatrist's assistance. In order to obtain a more valid idea of the extent of the first-year resident or intern's experience with the liaison psychiatrist, we inspected the total requests for psychiatric consultation made in each of three years by every intern of the Osler Medical Service (1955–1958) (Figure 1). About one-fourth of our first-year medical residents call the liaison psychiatrist to see between 11 and 15 of their patients per year. At the other extreme, around one-third of the first-year residents call the psychiatrist to see five or less of their patients under the same circumstances. Two-fifths of first-year residents request con-

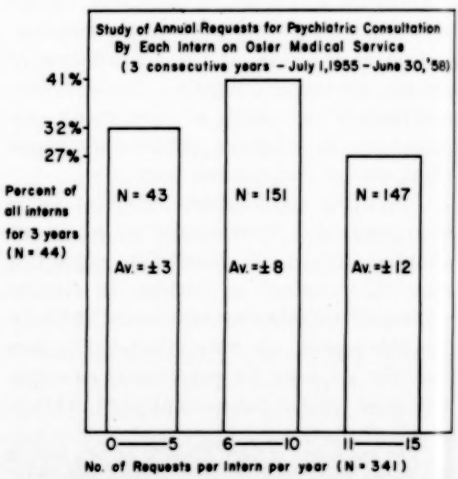
Study of Annual Requests for Psychiatric Consultation
By Each Intern on Osler Medical Service
(3 consecutive years – July 1, 1955 – June 30, '58)
41%
32%
27%
Percent of all interns for 3 years (N = 44)
N = 43
Av. = ± 3
N = 151
Av. = ± 8
N = 147
Av. = ± 12
0——5
6——10
11——15
No. of Requests per Intern per year (N = 341)

FIG. 1. Summary of interns' requests for psychiatric consultations.

sultation for six to ten of their patients. The average experience with the liaison psychiatrist of the "middle" and "high" request groups of interns (two-thirds of the total) comes to around ten patients during their medical ward experience. This does not, of course, include the medical intern's experience with the liaison psychiatrist in the out-patient department or in the emergency or overnight ward. We believe that this gives the majority of first-year residents a substantial experience with what a psychiatrist is and does in a variety of patient situations. When one clinician freely and of his own choice asks help from another physician, a specialist, for some aspect of the care of his patient, both physicians are apt to learn something. This is especially likely to occur when, as in the period of special study, there was an average of five discussions between the psychiatrist and the medical resident for each of the 60 consultations.

Beyond these descriptive data, it should be mentioned that a liaison psychiatrist tends to build up a kind of "practice" among the resident physicians. In several instances, collaborative and friendly relationships with particular residents are established in which a great deal of mutual respect and understanding result from the sharing of responsibility for interesting and difficult clinical problems. For the liaison psychiatrist, these experiences tend to offset those in which expressions of hostility and contempt for psychiatry, however, understandable in terms of "defenses," have their inevitable impact on the equilibrium and enthusiasm of the consultant.

SUMMARY AND CONCLUSIONS

An attempt has been made to evaluate the efficacy of the liaison psychiatrist in post-graduate teaching of medical residents. Within the framework of an established and functioning medical-psychiatric liaison service, we have made an intensive study of 60 consecutive spontaneous requests for psychiatric consultation by medical residents of the Osler Medical Ward Service of The Johns Hopkins Hospital (1954–1955). Certain data from this study were compared with the records of the liaison service from the period 1955–1958.

Of the total medical ward population of an "acute" medical service, a consulting psychiatrist was asked to see 8.8 per cent of all patients. This rate of request for psychiatric consultation does not differ significantly from the non-study years when able and interested liaison psychiatrists were answering requests for psychiatric consultation.

An analysis was made of requests for psychiatric consultation by each first-year resident ("intern") for three successive groups of interns (1955–1958)—a total of 44 interns. Thirty interns (68 per cent) requested between six and 15 consultations during their service on the medical wards. (Total: 299 consultations; an average of ten requests per intern). Fourteen interns requested between zero and five consultations during the same period. (Total of 43 consultations: an average of three requests per intern).

We conclude that the liaison psychiatrist can make a contribution to the post-graduate education of a substantial majority of medical residents.

REFERENCES

1. Erikson, E. H. The problem of ego identity. J. Am. Psychoanalyt. A., **4**: 56–121, 1956.
2. Fox, R. C. Training for uncertainty. In *The Student-Physician*, Merton, R. K., Reader, G., and Kendall, P. L., eds., p. 207. Harvard Univ. Press, Cambridge, 1957.
3. Kaufman, M. R. Role of psychiatrist in general hospital. Psychiat. Quart., **27**: 367–381, 1953.
4. Lidz, T. and Fleck, S. Integration of medical and psychiatric methods and objectives on a medical service. Psychosom. Med., **12**: 103–107, 1950.
5. Mendelson, M. and Meyer, E. The request for psychiatric consultation. To be published.
6. Meyer, E. and Mendelson, M. The psychiatric consultation with patients on medical and surgical wards: Patterns and processes. To be published.

LINDZEY, GARDNER, ED. *Assessment of Human Motives.* Rinehart and Company, New York, 1958. ix + 273 pp. $5.00.

The eight papers which make up this volume, plus an introductory chapter by the editor, were initially presented at a conference on the title topic held at Syracuse University. When the authors were invited to take part, their attention was directed to a number of problems in the area of assessment and they were asked to discuss as many of them as they cared to. These include the relative importance of conscious and unconscious motives and of direct and indirect methods of assessment, the role of cognitive control, situational variables and past experience, the need for more refined measures of known motives as opposed to the identification of additional ones, the value of focussing on a few motives as opposed to an appraisal of many, the value of detailed case studies as opposed to large scale controlled experimentation, and, finally, the value of animal research for the understanding of human motivation.

The authors, of course, vary considerably in the amount of attention they give to the problems mentioned. George Kelly, in the first paper, even throws out the concept of motivation altogether and substitutes one of "personal constructs." These constructs he sees as the means by which an individual organizes his world and they are the key to understanding the individual's behavior. He makes a strong case for considering the relevance of a construct before applying it to a person or an object, thus placing emphasis on situational factors, and also for considering the source of the construct rather than the object to which the source (person) applies it. Although he denies the relevance of the term, his is a highly cognitive approach. Kelly also denies the direct-indirect dichotomy, stating that interpreting an individual's words in terms of his construct system is no less "direct" than taking them at face value.

Leon Festinger devotes his paper to the development of a new variable, cognitive dissonance, as a motivating factor. He suggests and presents some very interesting supporting evidence that such dissonance produces efforts to reduce or eliminate it. His, too, is a cognitive approach.

George Klein is primarily concerned with cognitive style, which he defines as the characteristic way in which an individual goes about any activity, and which controls all expression of drives. Having a psychoanalytical orientation, he thinks primarily in terms of unconscious motives and attaches importance to past events.

In Roy Shafer's paper we find another which is devoted to a single concept, again a cognitive one: regression in the service of the ego. Shafer describes how this process may be used in evaluating not only analytic interview material but results from conventional tests. He closes his paper by stressing the importance of detailed studies of individuals as opposed to the generation of masses of correlations.

Irving Janis, after discussing some of the shortcomings of existing psychoanalytic research, gives some clear, concise, and cogent suggestions as to how the psychoanalytic interview can be used as an experimental research tool. He would thus bring the intensive study of the individual closer to the "experimental" approach.

Henry Murray develops a new concept, that of ascensionism, which he defines as a combination of need for achievement and need for awed attention and considers this a product of our way of life. He also discusses the detailed measurement of a large variety of needs and seems to place as much emphasis on direct as indirect measurement.

To no one's surprise, Raymond Cattell's chapter deals with multivariate analysis of

a large number of variables with a large number of subjects. Only in this way can the measurement of motivation be fruitfully undertaken, he feels. He, too, objects to the dichotomy of direct versus indirect measurement, insisting that a "direct" measure is one that gets to the heart of things. His basic unit of measurement is the attitude, expressed as an "I want," which suggests an emphasis on conscious motivation.

The final chapter by Gordon Allport discusses the units of measurement which have been used in assessment of the individual (beginning with the humors in the fourth century B.C.) and finds all of them wanting. For a new approach he urges a search for complex rather than molecular units, the acceptance of the notion of hypothetical constructs without the implication that because they are hypothetical they are fictional, and most importantly, the acceptance of variability of behavior from situation to situation. He makes a plea for improved ideographic analysis.

As the foregoing should suggest, this is a varied, fascinating, and very worthwhile collection for all who are interested in the area of personality dynamics.

Elizabeth G. French

ATKINSON, JOHN W., ED. *Motives in Fantasy, Action, and Society.* Van Nostrand Co., New York, 1958. xv + 873 pp. $9.75.

This encyclopedia of research information about achievement motivation bears two titles. The primary title, *Motives in Fantasy, Action, and Society,* is misleading. First, the main focus of this volume is not upon the social, theoretical, or practical implications of the operation of human motivation; second, only a limited number of motives is intensively considered (primarily achievement motivation, to some extent affiliation and power motivation). The subtitle of the book, however, is accurate in the extreme. This is given as, "A Method of Assessment and Study." It clearly describes the collection of careful, detailed research studies of methodological issues in the assessment of certain human motives that will be found therein. Professor Atkinson indicates this focus in his initial sentence, stating that, "The integrating theme of this book is the search for a method of assessment and study of human motivation . . ." (p. 1).

The observation that this collection of studies stresses methodological issues and the accumulation of empirical evidence to a greater extent than systematic theoretical considerations, is not offered as criticism. These investigators have attempted carefully reasoned theoretical presentations elsewhere (e.g., MCCLELLAND, ATKINSON, CLARK AND LOWELL. *The Achievement Motive.* New York, Appleton-Century-Crofts, 1953), and no single book can do everything. In any event, while motivation theory is not the central theme, it would not be accurate to say that no cogent and constructive theorizing appears in this book; Chapters 20, 22 and 42 are basically theoretical and the previews that Professor Atkinson presents in introducing the sections of this volume have theoretical implications. However, the real power of this book will be found in the methodological insights it provides.

Of the forty-six articles reported in this collection, the largest portion is contributed by "members of loosely organized teams or research seminars at Wesleyan or Michigan" (p. 3). Although Professor Atkinson appears somewhat embarrassed by this apparent provincialism (going out of his way to refer individually to those contributors whose primary identification is not with the Wesleyan-Michigan group), it would appear that it is precisely the provincial quality of the research program that generates its strength. This volume depicts great single-mindedness and direction in the solution of methodological issues in the assessment of certain human motives; such care, devotion, and detailed analysis can perhaps only be accomplished through this kind of collaborative, cooperative research attack.

The content of this book is accurately de-

scribed by the editor under six basic questions: "I. Does the arousal of motivation have any effect on the content of imaginative thoughts? II. What, in detail, is the nature of this influence? III. How do individual differences in the kind and strength of motivation influence behavior? IV. What factors influence the growth and development of a motive? V. Can content analysis of "thought samples" be employed to study problems of motivation in society? VI. How can thematic apperception measures of motivation be improved?" (p. vii). Many of the studies addressing these questions in this volume have appeared previously in journals; however, a goodly number (by, for example, McClelland, French, Atkinson, Winterbottom, etc.) appear here in print for the first time.

There are, of course, gaps or limitations that should be noted. Although there is much evidence presented concerning the achievement motivation of men in industry, men in mental hospitals, ubiquitous sophomore college men, etc., data concerning the assessment and operation of achievement motivation in women is virtually nonexistent. Again, one cannot condemn Doctor Atkinson and his colleagues for not having done all there is to do in this research area. However the appropriateness or usefulness, with samples of women, of the motivation assessment techniques examined by these researchers remains almost entirely unsettled. Also, no attempts to replicate the more critical research findings with men are reported. Lastly, and this observation will not be news to these researchers, only one measurement approach has been carefully and thoroughly appraised; the thematic apperceptive technique for assessing motivation (which requires the subject to produce imaginative stories in response to picture stimuli) is the only approach considered in detail.

However, these are quibbles when compared to what this volume accomplishes. It represents collaborative, scholarly research of high quality. It integrates these research findings around synthesizing issues. It has a clear purpose and direction and adds up to something. For any scientist with an interest in the multiple nuances of achievement motivation or in the general issues involved in the measurement of motivation, this book will be an invaluable resource.

Gerald S. Lesser

Although the two volumes reviewed above represent the thinking of a number of authors on the same topic—motivation and its measurement—the results are quite different. Professor Atkinson's book centers primarily on the characteristics of motivation as measured by the interpretation of fantasy material and on this technique of measurement itself. The various articles are highly interrelated and most of the authors have collaborated with or been otherwise associated with one another at some time. This volume represents a comprehensive analysis of basic methodological issues in a particular area of motivation theory. Professor Lindzey's book, on the other hand, is made up of papers by eight psychologists who have developed theories differing widely in perception of problems of motivation and method of approach. Although Lindzey, as editor, suggested a common starting point to the authors, the effect of this suggestion is not noticeable to the reader, and the book is perhaps all the fresher and more interesting because of that. One is given a varied view of current thinking over a large segment of the area of motivation. Thus, the two books have different purposes. Doctor Lindzey's book presents a variety of disparate theoretical views concerning motivation; Doctor Atkinson's book presents the work of researchers who start from a common theoretical base and attack a variety of methodological issues in the study of motivation. Both books serve their purposes well.

E. G. F.
G. S. L.

MANNHEIM, KARL. *Systematic Sociology: An Introduction to the Study of Society* (Eros, J. S. and Stewart, W. A. C., eds.). Philosophical Library, New York, 1958. xxx + 169 pp. $6.00

By the time of his death in the late nineteen-forties Karl Mannheim had achieved great renown as a leading social theorist and sociologist. In the decade or so which has followed, though, it is sad to note that much of this richly deserved reputation has become obscured, and nowadays one reads fewer and, for the most part, only passing references to the important body of writing bearing his name. While his two masterworks, *Ideology and Utopia* (1929) and *Man and Society in an Age of Reconstruction* (1940) would doubtlessly still be numbered among the most significant contributions to present-day political sociology and moral philosophy, it is perhaps no secret that these no longer generate the same enthusiasm and sense of bold intellectual adventure that they did at the time of their appearance. Quite apart from the purely assimilative effects wrought by time, the reasons for the current neglect of Mannheim's work are probably severalfold. In part they have to do with the emergence of other "grand style" sociological theorists who have captured the discipline's fancy. In part, this reviewer would hazard, the neglect is related to the growing disenchantment of intellectuals in general with the burning political issues, idealogical polemics and social reform movements that so bestirred this class through the decades of the thirties and forties, up to the full blown advent of the Cold War with its terrible restriction of viable political alternatives and competing points of view.

For it was essentially in the broad realm of the political that Mannheim's great scholarly resources and powers of analysis were most evident. Schooled in the great continental tradition of Marxian analysis and criticism, and having personally experienced a profound uprooting and transplanting from his native Germany to England when the Nazis came to power, Mannheim in his later and most productive years directed his energies toward illuminating the fundamental dilemma of democratic statecraft in the modern epoch, *viz.*, given the seemingly irreversible and mandatory trend toward greater centralized control and bureaucratic planning in industrial society, how can individual freedom and fulfillment best be preserved and advanced? With the possible exception of Karl Popper's treatise on the *Open Society*, no prior or subsequent analysis of this question matches in breadth or depth that to be found, for example, in Mannheim's *Man and Society*.

It is then cause for particular disappointment and regret for this reviewer to state that the present volume, published posthumously in Mannheim's name by two former students, does nothing to sustain, much less reinvest, the once considerable reputation and following enjoyed by this seminal and comprehensive thinker. Not only does *Systematic Sociology* bear little relation to that for which Mannheim is known, but in and of itself it is barely more than a facile, fragmentary and inadequately worked-through descriptive compilation of sociological concepts and categorical distinctions. Indeed, one wonders whether, had he a choice in the matter, Mannheim would have wished to have had these overly introductory, and probably somewhat perfunctory, classroom lectures and notes (the large bulk of which date as far back as 1934–35) edited and strung together in book form by Professors Eros and Stewart. Mannheim, we can assume, is not the only scholar who has been posthumously dealt a disservice by well-meaning former students, but in the present instance—and on the basis of what Mannheim himself chose to publish during his lifetime—one is further led to conjecture how much of what appears here is Mannheim's own and how much the improvisatory handiwork of his editors, a

matter not made entirely clear in the latter's editorial preface.

As presented, the volume purports to be a systematic inquiry and analysis of the several levels of individual and group behavior necessary to explain "the forms of living together of man, the sum of which we call society" (p. 1). In somewhat less than 150 pages the reader is rapidly and carelessly led through a sequence of conceptual definitions and categorical assertions on such awesomely complex topics as man's psychic equipment, elementary social processes, social integration, social change, etc., the narrative only rarely making provision for an apt illustration, a question, further elucidation or the consideration of an alternatively hypothesis. (If this in fact accurately reflects the style and substance of Mannheim's classroom lectures, we can have only the profoundest sympathy for those who were his students.) As might be expected of unrefined course materials, much that appears is transparently derivative and oversimplified, thereby imparting to the whole of the volume an unfortunate quality of catch-as-catch-can eclecticism. This will be readily apparent to readers of this journal in the section titled "Man and his Psychic Equipment," wherein Mannheim compounds a toxic amalgam of psychoanalytic, behavioristic and symbolic interactionist concepts, no one element of which does justice to the theory whence it derives, much less to man.

Occasional morsels redolent of better Mannheimian fare are reassuringly interlarded here and there, as for example in the discussion of estrangement from and sudden repossession of the self (p. 55) and the various forms of expansion of the self occuring through socialization (pp. 74–75), though these too are offered in a frustratingly terse and adumbrated manner. But a few morsels hardly make a meal, and when the host is someone at whose table one has formerly feasted, memory would have been better served in not having been invited at all.

Fred Davi

Annual Review of Psychology, Vol. 10. FARNSWORTH, P. R., ED. Annual Reviews, Inc., Palo Alto, 1959. 529 pp. $7.00

The tenth volume in this series of yearly reviews, systematically covering the current psychological literature, maintains the high merit and usefulness of its predecessors. The nonprofit corporation responsible for this enterprise now publishes *Annual Reviews* in nine major fields of science, of which three (*Biochemistry*, now in its 28th volume; *Physiology*, 21st volume; *Microbiology*, 13th) have a longer history than *Psychology*.

The present volume reflects an ongoing change in topical arrangements which will not be completed until 1961 (Volume 12), by which time certain chapter topics will appear yearly, others every other year, and some few others less frequently. Selection of the experts to prepare the different chapters will continue to be made several years in advance.

Each of the seventeen chapters in this book presents the boiled-down, doubly-distilled essence of some 150 articles (themselves selected from much larger numbers), critically evaluated by an expert. A notable bonus in this volume is an added chapter reporting on the state of psychology in Russia. Properly to review such a collection of reviews—and to find a reviewer so boldly omniscient as to essay it—is clearly impossible. One can do no more than to underline the admirably time-saving usefulness of such a book, particularly to those engaged in research and teaching. Chapter topics are written at a level which assumes a certain sophistication and background knowledge; this would certainly not be a safe way to begin to explore unfamiliar ground. But for the teacher or research investigator who

does not have the time to find out for himself—widely and at the source—what is going on in the areas of his interest, this is a most valuable book, a must.

H. A. Robinson

MORRISON, L. R., COBB, S. AND BAUER, W. *The Effect of Advancing Age upon the Human Spinal Cord.* Harvard University Press, Cambridge, 1959. 127 pp., illus. $6.00

This well-printed book offers an attempt to depict the histology of the "normal" human spinal cord at different ages as observed in "normal" autopsy material (rather than a discussion of the possible "aging" of this organ). The description is based upon the study of 31 spinal cords, using routine histological techniques. This task is as difficult as important, since the thus acquired knowledge represents an important step towards the establishment of a base line necessary for fruitful study of the pathology of the spinal cord.

Although interesting to read, as can be expected, the text asks a great effort on the part of the reader in order to unearth the essentials. This holds true also for the discussion which summarizes the findings of this study in terms of the histological elements involved: the meninges, the central canal, the myelin, the blood vessels, the spinal roots, the neurons, and the glia elements. These shortcomings in all likelihood are due to the untimely death of the senior author and could undoubtedly be corrected in a second edition. The same might apply to some unclear statements like "enerustation of the Golgi net" (Fig. 6). From a neuroanatomical point of view the nomenclature is sometimes vague.

In addition to the histological description of the spinal cord as observed at different ages, an atlas comprising cross-sections of 31 spinal segments is included. In this atlas the main emphasis is on the large cell groups of the anterior horn, especially in respect to cell counts. In the diagrammatic representation of the sections little attention has been paid to the structure of the rest of the cross section. A more detailed representation of the cross sections would undoubtedly have been a great asset to the book in its present form and, moreover, would have made it interesting to a greater number of readers.

In spite of shortcomings of this kind, however, the book is undoubtedly of importance and is seriously recommended to everybody interested in the normal and pathological anatomy of the central nervous system and especially in that of the spinal cord. This reviewer would hope that this book may stimulate the interest in this area of neuropathology too frequently neglected.

H. G. J. M. Kuypers

NOYES, A. P. AND KOLB, L. C. *Modern Clinical Psychiatry,* 5th ed. W. B. Saunders Co., Philadelphia, 1958. ix + 694 pp. $8.00

While there are a number of textbooks of psychiatry published in the United States, Noyes' *Modern Clinical Psychiatry* continues to be one of the few examples of excellent textbook writing. This volume not only covers the fundamentals of clinical psychiatry but gives a broad perspective for any one interested in the field. This new fifth edition, in which Dr. Kolb has collaborated with Dr. Noyes, brings the material of the fourth edition up-to-date.

The first six chapters have been little changed and remain a good frame of reference from which the physician, as well as other interested people, can view clinical psychiatry.

While subtle in character, one of the more significant changes in the present edition has been made in relation to more dynamic and personal dealings with the patients and the material. A modification of Chapter Seven in the section on examining the patient is a good example of this trend.

In the fourth edition the reader was advised immediately to obtain his history from the relatives, and then to see the patient. In this present edition the reader is advised to see the patient first and to develop a relationship which can be used in the future for therapy. In Chapter Eleven, "Mental Disorders Caused By Or Associated With Head Trauma," emphasis placed on the psychological response caused by the initial defect improves the understanding of head injuries from the psychiatric point of view. The sections on "Involutional Psychotic Reactions and Affective Reactions" are modified so that a more dynamic point of view is included. The section on "Schizophrenic Reactions" continues to be comprehensive but is presented less didactically, *e.g.*, the four A's of Bleuler are merged into the context of the discussion rather than being used mainly as a mnemonic device. The section on psychophysiologic reactions is rearranged and some parts have been rewritten. Cognizance is taken of some of the conflicts around the concept of psychosomatic medicine, but, because of the disagreements centering on the use of this concept, the general presentation is not completely satisfactory. Discussions of specific psychosomatic reactions are very effective, in the reviewer's opinion. In rewriting the section on psychopathic personality more dynamic explanations are now offered.

Two chapters have been added to this edition. A chapter on drugs fills a great need, since the last ten years have seen remarkable changes in drug therapy in psychiatry. For the future, this chapter might best be organized in terms of structural families of drugs rather than individual compounds. The other added chapter has to do with psychiatry and the law—a welcome addition. It is not only helpful in dealing with specific problems of hospitalization, but also in giving some background for the psychiatrist who is more frequently appealed to for advice in the psychological implications of legal matters.

Some new case material has been included to illustrate the revised contents. Sections have been added on hypoglycemia, Lupus Erythematosis, congenital galactosemia, porphyria and obesity. Discussions of the musculoskeletal system and respiratory reactions have been extended. Additions to the section on nervous system reactions have been made. The introduction of the phantom limb material well illustrates the body-image concept, which is an important addition. The section on phenylpyruvic acid deficiency has been enlarged and serves to underline attention directed to physiologic defects causing mental illness. The section on child psychiatry has been expanded with more case material.

Some of the detailing of gross and microscopic pathology, clearly irrelevant to a book of this type, has been left out. It is unfortunate that some of the older methods of treatment have been deleted to make room for consideration of new drug treatments. This reviewer was disappointed to find almost no mention made of hydrotherapy and older medications which can still be useful.

While this volume remains Doctor Noyes' classic, one can also note the salutary influence of the junior author. This edition maintains the high standards set by the earlier editions and can be highly recommended to medical students, physicians, and laymen interested in psychiatry.

Raymond I. Band

STEIN, H. D. AND CLOWARD, R. A., EDS., *Social Perspectives on Behavior*. The Free Press, Glencoe, Illinois, 1958. xix + 666 pp. $7.50

A a "... reader in social science for social work and related professions," this volume sets out to renew a long-neglected fellowship between the social sciences and psychodynamically oriented practice disciplines. This is a laudable, and in the opinion of this reviewer, a necessary step toward deeper understanding of interacting

Man and his groups. Too often dismissed by practitioners as "academic," that is to say, unrelated to practice and therefore impractical, many of the works of social scientists are clearly shown in this interesting book to be definitely part of what might be considered a practice-academic continuum. If a mother science is to be acknowledged for the broad field of human relations, Stein and Cloward appear to have given a hearty "Aye" to sociology. They obviously see evolving practice as being related to evolving social theory, one complementing rather than antagonizing the other.

The purpose of this book, "... to enable both the student and the experienced social worker—as well as the teacher, psychologist, and psychiatrist—to familiarize himself with concepts and findings in the social sciences which are relevant to professional practice," however, must have imposed a severe burden on the editors. As they undoubtedly realized, different levels of reader sophistication require different levels of explanation. Thus, the student or beginning social caseworker, for example, might require more detailed editorial explanations than would, say, the advanced social work practitioner, or the psychologist with a Ph.D.

In what could understandably have been their eagerness to include as many brilliant selections as possible in the 666 pages utilized, the editors may have compromised somewhat in their own space allotments. In any event, the impression gained at times during the reading of this book was that little more than cursory explanation was available to the neophyte concerning the relevance of some of the selections to practice. For such readers, there may be a tendency toward either gullibility or baffled estrangement. For the more sophisticated reader, however, the editors' awareness of the important implications for practice seems to be explained sufficiently in their introductions to the various sections. But more important, these implications stand out graphically in the texts of most of the chosen writings themselves.

One general pitfall which obviously could not be avoided in view of the nature of the book consists of possible confusion between individual and collective frames of reference. An approach to Man as a person will for some, perhaps conflict with understanding Man as the ever-changing product of and at the same time, the contributor to, his own ideals, values and beliefs which form and are formed by human interaction. Such conflict might be especially epitomized among psychiatrists and other psychotherapists, steeped as many of them are from their very professional beginnings in psychodynamics and individual psychopathology. On the other hand, acquiring this flexible perspective may be one of the rewards available in this work. There is really no reason why individual and collective points of view need to be mutually exclusive.

In fact, although it is agreed that the practitioner's viewpoint is by its nature different from that of the academician or social scientist, issue must be taken with the admonition on p. xviii of the Preface that, "the practitioner should be careful to retain his perspective as a practitioner, rather than regard himself as a social scientist. He does not have to be a social scientist to be a good practitioner."

In the broadest sense, every successful human being is at least an amateur social scientist and social theoretician. He has to be to survive. The magic of the words "science" and "theory" needs to be more favorably dispelled for practitioners toiling in the backwaters and brambles of Man's inhumanity to himself. It is the contention of this reviewer that practitioners in the broad field of human relations need to be better social scientists if their practice is to improve. Otherwise, books such as this one might create more practice problems than they assuredly are bound to solve.

Science is, after all, merely attempted explanation. In the social sphere, human in-

teraction being the effervescent bubbling pot that it is, practitioners as well as the social scientists are constantly attempting to explain. For explanation to be effective, a certain amount of contemplation is required. Contemplation is another basic meaning for theory which, according to some, is at its core a generalization, or conceptualization relating past observation and experience to the present in order that the future may be predicted within acceptable limits of probability. As such, social theory lends understanding to what would otherwise be a collection of mere sensory impressions.

All humans are constantly engaged in these processes of contemplation and explanation. Different to a great degree from the physical sciences, the social sciences are much more characterized by opinion rather than fact, erudite and disciplined as this opinion may be. It remains true that a fact in the physical sciences bears little resemblance to a social fact. Where a theory in the physical sciences may rest on laws, in the social sciences there are still few if any laws in the strict sense of the word. These and other matters could have been clarified more effectively for the less sophisticated reader. For example, some of the weaknesses of some of the theoretical viewpoints might have been mentioned by the editors in order to avert too uncritical reader acceptance of opinions which appear to be facts.

Beginning with Family Structure and Ethnic Patterns, this text proceeds through readings on Social Roles, Values, Social Stratification, Deviant Behavior as a Property of Groups, and concludes with a consideration of Bureaucratic Structure. In this development, a theme from the relatively simple to the complex is obvious. As the reader warms up this theme, new ideas find sustenance in what has been read. The continuity which is comfortably apparent is in itself a tribute to the careful editorial selection effort which must have gone into producing it. The erudite conceptualizations available in the various contributions illustrate time after time the difficult and changing *milieu* of patterns and systems which characterize humanity. But best of all, the plethora of work left and accumulating for the practitioner begins to take on shape and form in its very segments, opening avenues for more effective approaches to the multiple problems at hand.

Had this reviewer been in a voting role as to selections to be included, some of the work of Wirth and Redfield would have been added, as well as that of Cooley and Faris, with reference to understanding the continuum of Urban-Folk and Primary-Secondary Group interaction patterns. (Note how the book proceeds from Family to Bureaucracy.) Also, instead of the clumsy, mechanical stumbling block of having to turn to the back of the book for footnotes and other comments, it would have been vigorously voted that these appear on their appropriate pages.

If one unequivocally positive statement is to be made concerning this healthy and admirable effort, it is related to the specificity of the selections. Practitioners seeking specific help in understanding a specific clientele or subgroups of their case-loads, will find great help in this book. Nevertheless, it is not suggested that it be used in this manner. The rewarding and impressively fulfilling experience for all those interested and involved in more effectively channelizing human interaction is to be found by reading it completely from beginning to end, including notes as they appear. Theory and Science and Practice subtly find their similarities amidst their differences in the reader's mind as he journeys through its pages.

Anthony R. Stone

MASLAND, R. L., SARASON, S. B. AND GLADWIN, T. *Mental Subnormality*. Basic Books, Inc., New York, 1958. 442 pp. $6.75

This volume comprises two reports representing different facets of, and widely differing approaches to, a single survey. The first and briefer section (144 pp.), by Dr. Masland, presents a review of research on biological factors in mental subnormality. It includes, among others, discussions of pathological studies, prenatal and postnatal determinants, and surveys of incidence. Part II, by Doctors Sarason and Gladwin, deals with psychological and cultural factors, and in effect is an attempt to determine how much is known about these broad areas of etiology. What follows is a review of Part II (pp. 145–442) of this volume. Ed.)

Those who are interested in the varieties of behavior subsumed by the term "mental deficiency" may be divided into two general schools. The first of these does not recognize in theory or practice that mental deficiency is a variety of syndromes, and that the higher grade defect may well present a special problem demanding the combined skills of sociologists, cultural anthropologists and personologists. For this group of traditionally minded workers, genetics and constitutional etiological factors are primary, and scant attention is given to other causes. Wide varieties of behavior are typically explained as follows: "He steals because he doesn't know any better." The "traditionalists," if required to explain the frequently peculiar behavior of lower-grade defectives, will continue to involve purely constitutional hypotheses. Psychotic-like behavior and hyperactivity are subsumed as manifestations of brain damage. Deeper probes into such behavior are not sought. In the all-important applications of theory to such issues as training, socialization, and education; the traditional approach persists with the shibboleths of sense-training, repetition, habit training, etc. This represents a flattering if not outdated adherence to the contributions of Itard and Watson, to the exclusion of later theorists.

It is possible that this description of those who work with mental defectives may be a cardboard giant. However, this reviewer feels that it is generally representative of the thought of many who are responsible for the care of mental defectives in large state institutions. Perhaps even more meaningfully, these attitudes will be recognized as being frequently held among psychiatrists, clinical psychologists and others who devote their energies to the study and treatment of intelligent neurotic and psychotic patients. For these workers, research, theory and practice within the area of mental retardation is a near-hopeless task and one often avoided because of the generally accepted genetic and constitutional etiological theories.

The second school of through may be characterized as having a functional bias. Those workers, who—perhaps out of need for optimism, or because of sheer boredom—concern themselves with a non-constitutional approach, have been frustrated in searching the literature for ideas, data, or inspiration. Of the few books which avoid the clichés of our scientific past, the volume reviewed here is easily the most comprehensively well-documented and most thought-provoking book published to date. (Incidentally, for those wishing a fuller exposition of Dr. Sarason's views of mental deficiency, the monograph reviewed here is also included as a part of the third edition of his *Psychological Problems in Mental Deficiency*, Harper & Bros., New York, 1959.)

In purpose the book is double-barreled. There is, first, a selected review of the pertinent literature. Second, there are stated and discussed, as usable hypotheses and as guides to action, several conclusions which are based upon the review.

The chapters are entitled:

1. Introduction to the Psychological and Cultural Factors.
2. The Uneducated.
3. Problem-solving Behavior in Non-test Situations.
4. "The Structure of Intellect".
5. Heredity and Environment.
6. Cultural Background Factors Affecting Test Performance.
7. Intelligence and Culture.

8. The Severely Defective Individual.
9. The Higher Grade of Mental Defect.
10. Recommendations.

These descriptive chapter headings indicate of themselves the importance attributed to cultural factors in the definition of retardation. The point is made in discussing Goddard's research with the Kallikak family that "... he failed to perceive that he was describing an environment *in itself* sufficient to explain the deficiencies of the Kallikaks without recourse to the hereditary deficit whose existence he believed he was documenting" (p. 298, italics added). While this quotation is neither a proof of an hypothesis nor in itself startling, it represents the beginning point of a line of argument to demonstrate an environmental (cultural or subcultural) etiology of deficiency. As one who has learned from and shares the authors' viewpoint, it must be mentioned how difficult it is to expound the hypothesis quoted above. Frequently this reviewer, in conducting seminars with professional people, has attempted to point out the possibility, for example, that the IQ is not simply a matter of heredity by utilizing this concept. That this quotation is not perceived, or quickly forgotten, or distorted, demonstrates the intensity of traditional beliefs regarding this scientific question.

As stated, part of the purpose of the reviewed book is to specify likely non-biological factors determining mental retardation, as derived from the available literature. The arguments and research of the geneticists have not been reviewed, and to this extent the monograph represents a consciously biased approach. Perhaps the true value of Part II of this volume is to forcibly demonstrate the necessity for changing frames of reference and to suggest concretely areas of research likely to prove productive.

While social and clinical psychologists have in general been well aware of the cultural bias of traditional intelligence tests (presumably arising out of a need to understand inter-race and international IQ differences), the implications of this for mental retardation have been largely ignored. That a neglected, deprived child from a disintegrated family background is often unable to verbalize freely, or to assemble blocks so as to reproduce a design skillfully, has caught the attention of social and clinical psychologists. But rarely have the theories and experiences of both disciplines been combined as they have been in this book.

Doctors Sarason and Gladwin raise the issues of individual motivation, cultural differences in whether learning is to be valued *per se*, the cultural variation in incentive systems, etc., as vital in IQ testing and in the diagnosis of mental retardation. Indeed, the genesis of value systems, the desire to learn and the cultural content of what is learned, together make up a central theme of the book. The position is taken that some varieties of high grade defect represent a cultural emphasis (or lack of it), and not innate lack of capacity.

One of the more interesting sections of *Mental Subnormality, Part II*, is concerned with severe defect, in which organic pathology and psychotic-like behavior patterns are reviewed. Problems presented by the idiot savant, the autistic child, and by idiots with psychotic-like symptoms are approached from several theoretical positions. The point is astutely made that the study of such pathology may inform personality theorists about normal processes (in the same way, perhaps, as Freud's study of selected abnormal behavior generated an entire body of psychological theory).

For workers in the field of mental deficiency, and all interested others, this book is surely required reading. Herein lies a stimulating and comprehensive body of data and ideas.

Gerald Wiener

LETTERS TO THE EDITOR

Dear Sir:

In the January, 1959, issue of this Journal A. Hoffer and H. Osmond have presented data purporting to represent the concentration of adrenochrome in the plasma of various subjects. Last December we received, through the courtesy of Dr. Hoffer, the essential details of the method employed at the University Hospital, Saskatoon, for measuring adrenochrome, and were able to examine the procedure in the biochemical research laboratory of the Department of Psychiatry, McGill University. The method, described by A. N. Payza and M. E. Mahon, has now appeared in Analytical Chemistry, **31**: 1170–1174, 1959. We wish to report upon our experience with this method.

The principle of the method lies in the extraction of plasma with acetone, and the conversion, by means of zinc acetate, of the extracted adrenochrome to its fluorescent isomer, adrenolutin. The intensity of the fluorescence is related to the concentration of adrenochrome by carrying standard solutions of this substance through all steps of the procedure. Plasma to which has been added a sufficient quantity of authentic adrenochrome (kindly donated to us by Dr. R. A. Heacock) yields an extract exhibiting the characteristic activation and emission peaks of fluorescence. Recovery of added adrenochrome is of the order of 70 per cent.

Payza and Mahon recommend the use of two types of blank. One consists of extracted plasma but omits the zinc acetate reagent; the other consists of reagents, including zinc acetate, but no plasma. The fluorescence values of the treated plasma extracts are corrected for these blanks.

We have found that zinc acetate, together with the other reagents, yields substantial non-specific fluorescence at the recommended wave-length settings. Using this "blank" correction we estimate the fluorescence due to "adrenochrome" in plasma drawn from schizophrenic and normal subjects, as being zero or negative. The reagent presumably suppresses the fluorescence of native fluorophors in the plasma, or it develops fluorescent materials itself. Furthermore, we have examined all plasma extracts for the characteristic activation and emission spectra of adrenolutin. In no sample of plasma did we find these. In fact, the fluorescence of the extracts in the environs of the wave-lengths used for measuring adrenolutin is quite flat and non-specific. In our work we used the Aminco-Bowman Spectrophotofluorometer; the Saskatchewan group made their measurements with the Farrand model. It is highly unlikely that differences in results of the order of magnitude found would arise from instrumental variation. Needless to say, we have made all fluorescence measurements well within the time limits prescribed by Payza and Mahon, and we have paid special attention to their warnings about purity of reagents.

In summary, the present results contradict those reported in your Journal by Hoffer and Osmond, and raise the question: What precisely was it they measured?

This work was supported by Federal-Provincial Mental Health Research Grants to Dr. R. B. Sloane, Dr. R. A. Cleghorn and Dr. T. L. Sourkes.

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Dear Sir:

Hoffer and Osmond (J. Nerv. & Ment. Dis., **128:** 18–35, 1959) in a review of the adrenochrome hypothesis of schizophrenia

referred to a method for measuring adrenochrome developed by Payza and Mahon (Anal. Chem., **31:** 1170–1174, 1959). Layne and Sourkes properly ask the question, "What precisely was it they measured?"

It is clear that biochemists, writing as biochemists, even more than biochemists writing as psychiatrists, must shoulder some responsibility in seriously examining biochemical matters which may vitally affect the course of psychiatric research.

I do not propose to examine in detail the query raised, because Payza and Mahon made it amply clear what they were measuring when they wrote, "Because neither adrenochrome or any of its derivatives have yet been isolated from blood or urine, there is no absolute proof that this method measures adrenochrome. However, the method is accurate when adrenochrome is added to plasma or injected intravenously into blood. Plasma contains fluorescent factors which behave as if they were adrenochrome. Therefore it is a working assumption that adrenochrome is being measured. However, proof must await isolation studies."

I would also like to know precisely what is being measured, but to achieve such precise knowledge may require much hard work.

Sourkes very briefly discussed this matter with me in March of 1959. At that time he reported that a blank consisting of zinc acetate together with other reagents yielded substantial non-specific fluorescence which increased with time. This led him to doubt whether adrenochrome was really present. To this I replied that Dr. Feldstein (1958) had made a similar observation and had raised the same interesting question in private communication. Feldstein later asked the same question during a discussion at the Conference on Amine Oxidase Inhibitors, New York Academy of Sciences (1959). This was possibly of great importance, but since this was not the blank used by Payza and Mahon it has little relevance here. The published method called for two types of blanks; 1) one which measures the degree of impurity in terms of fluorescent materials in the chemicals, and 2) one which measures the quantity of fluorescence naturally present in plasma (which may consist of numerous substances each of which contributes specifically to the overall fluorescence).

Layne and Sourkes report, as did Feldstein, that zinc acetate together with the other reagents yield substantial non-specific fluorescence (whatever that is). This would be a valid criticism provided that they could show that the same nonspecific reaction occurred when these reagents were added to plasma. In fact we have found that this "non-specific fluorescence" does not appear in plasma because the fluorescence readings are relatively stable (as was shown by Payza and Mahon).

With this blank, which we do not recommend, the fluorescent readings will eventially surpass the readings of solutions containing authentic crystalline adrenochrome. I would expect that if the solutions were allowed to stand long enough this particular blank would lead to negative values.

This we have discussed with Dr. Feldstein and we are grateful to him for bringing it once more to our attention because it has stimulated Payza and Mahon to improve the method. The new method uses a set of reagents where the total (all reagents) blank is used and which is stable several hours. Ascorbic acid is not required. Layne and Sourkes have merely confirmed Feldstein's and our own observations, made and accounted for when the method was first developed. By the time this communication appears the newer method should be available in Analytical Chemistry, to which I direct these authors' attention.

Layne and Sourkes deem it unlikely that instrument differences are responsible, and I agree. It is much more likely that the original method was not precisely followed but a new one developed, *i.e.*, a new blank, which may or may not be valuable. We would not be surprised if the Layne-Sourkes method shows no adrenochrome. However, it might

be useful to the reader to know that there are important instrument differences. These instruments require a rather constant line voltage of about 115 volts. In most hospitals voltage fluctuates considerably and is often below 115. Below 115 volts, the excitation intensity of the Xenon Arc Lamp is too feeble to give a proper excitation of the adrenolutin-zinc complex. We have overcome the difficulty by using a Type W20MT3 Autotransformer made by General Radio Company, Cambridge, Mass. between the line and the flourometer.

I think that the Layne and Sourkes method will be of limited usefulness, for they state, "the principle of the method lies in the extraction of plasma with acetone, and the conversion, by means of zinc acetate, of the extracted adrenochrome to its fluorescent isomer, adrenolutin." It is difficult to interpret this statement in the light of the known chemistry of adrenochrome. According to Heacock (Chem. Reviews, **59:** 181–237, 1959) adrenochrome is "fairly soluble in acetone." Adrenolutin is much more soluble in acetone and partitions better than does adrenochrome from the aqueous to the acetone phase. The Payza and Mahon method reads as follows: "The plasma (1 ml.) was placed in a 25 ml. Erlenmeyer flask and reagent 3 (2 ml. zinc acetate-ascorbic acid) was added and allowed to stand for 30 seconds. Reagent 5 (4 ml. acetone-ascorbic acid) was added with swirling and allowed to stand five minutes at room temperature to precipitate the plasma proteins *and convert adrenochrome into adrenolutin* (italics added)." Thus the reaction is completed before the addition of acetone. The italicized statement is incorrect in this context: the reaction occurs before the acetone is added. It is a simple matter for the authors to determine whether the adrenochrome is converted into adrenolutin before or after the addition of acetone reagent. I can only assume they have not followed the details of the method given to them before publication.

I hope your correspondents will not be discouraged from publishing the details of their new method in a biochemical journal.

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